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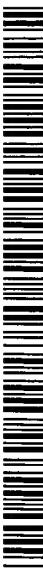
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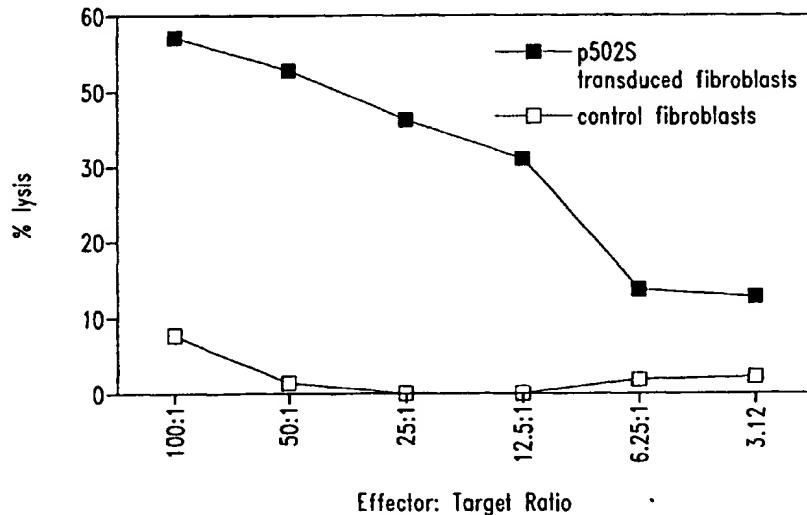
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(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



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(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.



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COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments,

5 the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the

10 foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

15 The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions

20 comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

25 The present invention further provides pharmaceutical compositions that comprise:

(a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with

30 monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5 Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15 Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

20 The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

25 Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

- The present invention further provides methods for inhibiting the development of a
- 5 cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.
 - 10 Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of

- 15 polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a

- 20 biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the
- 25 patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a

- 30 polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that 5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) 10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as 15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed 20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The 25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5 Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2K_b targets and P501S-transduced Jurkat A2K_b targets, as compared to EGFP-transduced Jurkat A2K_b. The percent lysis is shown as a series of effector to target ratios, as indicated.

10 Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2K_b cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

15 Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

20 Figure 8 illustrates the results of epitope mapping studies on P501S.

Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25 Figure 11 shows the results of an ELISA assay of antibody specificity to P501S peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

- SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
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SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
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SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
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15 SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
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SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
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SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
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SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
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SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

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- SEQ ID NO: 58 is the determined cDNA sequence for P60
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- SEQ ID NO: 66 is the determined cDNA sequence for P68
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SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781
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SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304
SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296
SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280
SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12
SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17
SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)
SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as
10 P503S)
SEQ ID NO: 112 is the predicted amino acid sequence for J1-17
SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)
SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)
SEQ ID NO: 115 is the determined cDNA sequence for P89
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SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6
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30 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762
SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766
SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770

- SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
- SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772
- SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309
- SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
- 5 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288
- SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
- SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
- SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
- SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
- 10 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
- SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
- SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
- SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
- SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
- 15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
- SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
- SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
- SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
- SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
- 20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
- SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
- SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
- SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
- SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
- 25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
- SEQ ID NO: 223 is the determined cDNA sequence for P509S
- SEQ ID NO: 224 is the determined cDNA sequence for P510S
- SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
- SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
- 30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
- SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
- SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

- SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

- SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

- SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
- SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
- SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
- SEQ ID NO: 297 is the determined cDNA sequence for JP8B10
- 5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10
- SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
- SEQ ID NO: 300 is the determined cDNA sequence for JP8E10
- SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
- SEQ ID NO: 302 is the determined cDNA sequence for JP8H9
- 10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
- SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
- SEQ ID NO: 305 is the determined cDNA sequence for JP8E12
- SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
- SEQ ID NO: 307 is the determined cDNA sequence for P711P
- 15 SEQ ID NO: 308 is the determined cDNA sequence for P712P
- SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
- SEQ ID NO: 310 is the determined cDNA sequence for P774P
- SEQ ID NO: 311 is the determined cDNA sequence for P775P
- SEQ ID NO: 312 is the determined cDNA sequence for P715P
- 20 SEQ ID NO: 313 is the determined cDNA sequence for P710P
- SEQ ID NO: 314 is the determined cDNA sequence for P767P
- SEQ ID NO: 315 is the determined cDNA sequence for P768P
- SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes
- SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5
- 25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
- SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
- SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
- SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
- SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
- 30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S
- SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)
- SEQ ID NO: 334 is the determined cDNA sequence for P714P

- SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo
10 sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin
- 15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo
20 sapiens phosphoglucomutase-related protein (PGMRP)
- SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- 25 SEQ ID NO: 352 is the determined cDNA sequence for P790P
- SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- 30 SEQ ID NO: 357 is the determined cDNA sequence for P745S
- SEQ ID NO: 358 is the determined cDNA sequence for P782P
- SEQ ID NO: 359 is the determined cDNA sequence for P783P

- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- 5 SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- 10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 15 374.
- SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- 20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- 25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- SEQ ID NO: 390 is the cDNA sequence for 23381.
- SEQ ID NO: 391 is the cDNA sequence for KIAA0122.
- SEQ ID NO: 392 is the cDNA sequence for 23399.
- 30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.
- SEQ ID NO: 394 is the cDNA sequence for HCLBP.
- SEQ ID NO: 395 is the cDNA sequence for transglutaminase.

- SEQ ID NO:396 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:397 is the cDNA sequence for PAP.
- SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.
- SEQ ID NO:399 is the cDNA sequence for hTGR.
- 5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.
- SEQ ID NO:401 is the cDNA sequence for 22545.
- SEQ ID NO:402 is the cDNA sequence for 22547.
- SEQ ID NO:403 is the cDNA sequence for 22548.
- SEQ ID NO:404 is the cDNA sequence for 22550.
- 10 SEQ ID NO:405 is the cDNA sequence for 22551.
- SEQ ID NO:406 is the cDNA sequence for 22552.
- SEQ ID NO:407 is the cDNA sequence for 22553.
- SEQ ID NO:408 is the cDNA sequence for 22558.
- SEQ ID NO:409 is the cDNA sequence for 22562.
- 15 SEQ ID NO:410 is the cDNA sequence for 22565.
- SEQ ID NO:411 is the cDNA sequence for 22567.
- SEQ ID NO:412 is the cDNA sequence for 22568.
- SEQ ID NO:413 is the cDNA sequence for 22570.
- SEQ ID NO:414 is the cDNA sequence for 22571.
- 20 SEQ ID NO:415 is the cDNA sequence for 22572.
- SEQ ID NO:416 is the cDNA sequence for 22573.
- SEQ ID NO:417 is the cDNA sequence for 22573.
- SEQ ID NO:418 is the cDNA sequence for 22575.
- SEQ ID NO:419 is the cDNA sequence for 22580.
- 25 SEQ ID NO:420 is the cDNA sequence for 22581.
- SEQ ID NO:421 is the cDNA sequence for 22582.
- SEQ ID NO:422 is the cDNA sequence for 22583.
- SEQ ID NO:423 is the cDNA sequence for 22584.
- SEQ ID NO:424 is the cDNA sequence for 22585.
- 30 SEQ ID NO:425 is the cDNA sequence for 22586.
- SEQ ID NO:426 is the cDNA sequence for 22587.
- SEQ ID NO:427 is the cDNA sequence for 22588.

- SEQ ID NO:428 is the cDNA sequence for 22589.
- SEQ ID NO:429 is the cDNA sequence for 22590.
- SEQ ID NO:430 is the cDNA sequence for 22591.
- SEQ ID NO:431 is the cDNA sequence for 22592.
- 5 SEQ ID NO:432 is the cDNA sequence for 22593.
- SEQ ID NO:433 is the cDNA sequence for 22594.
- SEQ ID NO:434 is the cDNA sequence for 22595.
- SEQ ID NO:435 is the cDNA sequence for 22596.
- SEQ ID NO:436 is the cDNA sequence for 22847.
- 10 SEQ ID NO:437 is the cDNA sequence for 22848.
- SEQ ID NO:438 is the cDNA sequence for 22849.
- SEQ ID NO:439 is the cDNA sequence for 22851.
- SEQ ID NO:440 is the cDNA sequence for 22852.
- SEQ ID NO:441 is the cDNA sequence for 22853.
- 15 SEQ ID NO:442 is the cDNA sequence for 22854.
- SEQ ID NO:443 is the cDNA sequence for 22855.
- SEQ ID NO:444 is the cDNA sequence for 22856.
- SEQ ID NO:445 is the cDNA sequence for 22857.
- SEQ ID NO:446 is the cDNA sequence for 23601.
- 20 SEQ ID NO:447 is the cDNA sequence for 23602.
- SEQ ID NO:448 is the cDNA sequence for 23605.
- SEQ ID NO:449 is the cDNA sequence for 23606.
- SEQ ID NO:450 is the cDNA sequence for 23612.
- SEQ ID NO:451 is the cDNA sequence for 23614.
- 25 SEQ ID NO:452 is the cDNA sequence for 23618.
- SEQ ID NO:453 is the cDNA sequence for 23622.
- SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
- SEQ ID NO:455 is the cDNA sequence for LIM protein.
- SEQ ID NO:456 is the cDNA sequence for a known gene.
- 30 SEQ ID NO:457 is the cDNA sequence for a known gene.
- SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:459 is the cDNA sequence for 23045.

- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- SEQ ID NO:468-471 are cDNA sequences for P710P.
- 5 SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO:
- 15 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO:
- 25 473.
- SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.
- SEQ ID NO: 485 is the PCR primer AW025.
- 30 SEQ ID NO: 486 is the PCR primer AW003.
- SEQ ID NO: 487 is the PCR primer AW027.
- SEQ ID NO: 488 is the PCR primer AW026.

- SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.
- SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.
- SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for
5 the anti-P503S monoclonal antibody JA1.
- SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.
- SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.
- SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for
10 the anti-P703P monoclonal antibody 7H8.
- SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.
- SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.
- SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO:
15 524 is the putative full-length cDNA sequence of P703P.
- SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.
- SEQ ID NO: 526 is the full-length cDNA sequence for P790P.
- SEQ ID NO: 527 is the predicted amino acid sequence for P790P.
- SEQ ID NO: 528 & 529 are PCR primers.
- 20 SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.
- SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.
- SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.
- SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.
- SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.
- 25 SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.
- SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.
- SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.
- SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.
- SEQ ID NO: 539 is the peptide P501S-370.
- 30 SEQ ID NO: 540 is the peptide P501S-376.
- SEQ ID NO: 541-550 are epitopes of P501S.
- SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also 5 encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the 10 present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions 15 and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The 20 term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local 25 regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the 30 Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example,

5 a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997).

10 Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

15 An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes.

20 Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into

a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally 5 performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

10 One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence 15 and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the 20 use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

25 In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

30 Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis.

5 Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain
10 portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

15 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression
20 through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of
25 the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30
30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

15 Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.
20 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary
25 skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane
30 vesicle). The preparation and use of such systems is well known in the art.

PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ^{125}I -labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the 5 protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

- Polypeptides may be prepared using any of a variety of well known techniques.
- 10 Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells.
 - 15 Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed
 - 20 to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase 25 synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that 30 comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted
5 to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly,
10 DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component
15 polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be
20 chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker
25 sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions
30 that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its

original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector
5 that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an
10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding
15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals
25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the
30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are 5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. 10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to 15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (*Monoclonal Antibodies and Cancer Therapy*, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by 20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the 25 desired biological activity, such as activation of human complement and mediation of ADCC (*Morrison et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; *Neuberger et al. Nature* 312:604, 1984; *Takeda et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may 30 be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, 5 drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

10 A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulphydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid 15 halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling 20 efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be 25 effected, for example, through amino groups, carboxyl groups, sulphydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is 30 cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

5 It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or
10 linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating
20 compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of
25 a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

30 Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated
5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific
10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell
20 proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of
25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN- γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4 $^{+}$ and/or CD8 $^{+}$. Prostate-specific protein-specific T cells may be expanded using
30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide 5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

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PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds 15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally 20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the 25 composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression 30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia 5 or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; 10 WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and 15 Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the 20 DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary 20 depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid 25 carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

30 Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA

or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12; may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent 5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release 10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix 15 and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical 20 compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the 25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or 30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

Ann. Rev. Med. 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells 5 with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of 10 the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical 15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. 20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react 25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not 30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate 5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in* 10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, 15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies 20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced 25 into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitory, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established 30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%
5 above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-
10 vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active
15 compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be
20 evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or
25 more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the
30 agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, 5 *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized 10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, 15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full 20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or 25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" 30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of 5 binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the 10 binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may 15 be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The 20 amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 25 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. 30 Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by

assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains 5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of 10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group 15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a 20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is 25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest 30 to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4 $^{+}$ and/or CD8 $^{+}$ T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may
5 be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater
10 and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to
15 amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization
20 assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in
25 length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15
30 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (see, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, 5 and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or 10 greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or 15 polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

20 Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

25 As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or 30 alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate
10 tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning
kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol.
Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and
total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the
manufacturer. The poly A⁺ RNA was then purified using a Qiagen oligotex spin column mRNA
15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-
strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was
synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with
NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the
cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into
20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was
prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by
determining the number of independent colonies, the percentage of clones that carried insert, the
average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7
25 independent colonies, with 70% of clones having an insert and the average insert size being 1745
base pairs. The normal pancreas cDNA library contained 3.3×10^6 independent colonies, with 69%
of clones having inserts and the average insert size being 1120 base pairs. For both libraries,
sequence analysis showed that the majority of clones had a full length cDNA sequence and were
synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal
pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some
modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA

library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 5 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further 10 analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the 15 identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 20 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4288, 1D-25 4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

30 cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and 10 P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S 15 are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as 20 P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using 25 Trizol reagent as described above. First strand synthesis was carried out using 1-2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed 30 using β-actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β-actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue
5 (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found
10 to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other
15 tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of
20 prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

25 RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors
30 and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following 5 normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues 10 tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in 15 normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in 20 prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and 25 expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney). The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was 30 found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal 5 antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis 10 of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, 15 and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

20

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with 25 ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). 30 DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences 5 for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the 10 isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161- 15 170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA 20 sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary 25 (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a 30 portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in 5 prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, 10 substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The 15 determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 20 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array 25 technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, 30 colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity 5 to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA 10 sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of 15 P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

20 Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 25 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal 30 prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the 5 cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence 10 being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no 15 significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ 20 ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. 25 The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 30 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

EXAMPLE 4

5 SYNTHESES OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to 10 the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in 15 water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

20

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC 25 POLYPEPTIDES BY PCR-BASED SUBTRACTION

25

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that 30 recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and SstI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in 5 prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low 10 expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 15 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID 20 NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels 25 in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

EXAMPLE 6
PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5 6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGVVVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID 10 NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100 μ g of P2S#12 and 120 μ g of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 10⁶ cells/ml in complete media (RPMI-1640; Gibco 15 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10⁻⁵ M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 μ g/ml dextran sulfate and 25 μ g/ml LPS for 3 days). Six days later, cells (5 x 20 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 3 x 10⁶/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb 25 tumor cells (1 x 10⁴ cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10⁵ cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in 30 Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice
5 were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994).
10 P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on
15 the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described
20 by Theobald *et al.* (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10⁶ cells/ml in complete media (as described above) and cultured
25 in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10⁶/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were
30 restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2K_b tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown 5 in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2K_b targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

10 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION
WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2K_b Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012 either intramuscularly or intradermally. 15 The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2K_b-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at 20 least one naturally processed HLA-A2-restricted CTL epitope.

EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

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This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van 30 Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ-interferon

ELISPOT assay (see Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10^4 fibroblasts in the presence of 3 $\mu\text{g}/\text{ml}$ human β_2 -microglobulin and 1 $\mu\text{g}/\text{ml}$ P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, 5 fibroblasts transduced with HER-2/neu. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed 10 with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/neu gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally 15 processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

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EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL 25 response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the 30 addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8 $^{+}$ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL
5 transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (^{51}Cr release) and interferon-gamma production (Interferon-gamma Elispot; see above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

10

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A
PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also
15 referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation
20 of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th
25 peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were
30 identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of 5 the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

EXAMPLE 11

10 EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN
IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in 15 SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in 20 SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly 25 expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

EXAMPLE 12

30 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND
STIMULATION TECHNIQUES WITH PROSTATE-SPECIFIC ANTIGEN

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described above. Using a panel of 5 HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a 10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that 15 specifically produced interferon- γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

20 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S 25 fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were 30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

25

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

5

Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of 5 prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is 10 not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of 15 normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 20 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It 25 was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It 30 was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

10

EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS
BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify
15 prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatzis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST
20 sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for
25 ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line
30 libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which

expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II
Prostate cDNA Libraries and ESTs

5

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for
5 Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as
10 described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

15 Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY
ANALYSIS

5

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened 10 using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

15

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

20 This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four
5 sequences were obtained, and are presented in SEQ ID NO: 468-471 These sequences appear to represent different splice variants of the P710P gene.

EXAMPLE 17

PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

a) Expression in *E. coli*

15 Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus
30 *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5 An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR
10 product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

15 The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands
15 were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

20 A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25 The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, 5 Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the 10 GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan 15 (Becton Dickinson), and the data were analyzed using the Cell Quest program.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

20 a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

25 A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using 30 ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to

generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were 5 generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

10

Table V
Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant (μ g/ml)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. 15 Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 μ g/ml, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of 20 infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the 5 surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 10 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody 15 specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in 20 Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as 25 P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of 30 normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach
5 was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and
10 subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L)Affinipure F(ab') fragment (Jackson Immunoresearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and
15 incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array
20 immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM
25 citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

30 **b) Preparation and Characterization of Antibodies against P503S**

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

5

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for
10 the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO:
502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series
of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These
peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows.
15 The recombinant fragment of P503S that was employed as the immunogen was used as a positive
control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at
20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline
containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1%
Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells
20 and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST
and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were
washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception
5 of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

10 Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat
15 anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis
20 was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary,
25 pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal
30 antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

5 **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal 10 antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptr1	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptr1	Rabbit monoclonal
8H2	P703Ptr1	Rabbit monoclonal
7H8	P703Ptr1	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal 20 antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk-/- cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed
5 with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

10 Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

15

EXAMPLE 19

CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen
20 P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that
25 following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains.
30 Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM

sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by 5 SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in LnCap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma 10 membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter 15 plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with 20 phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates 25 were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

30 In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as 5 described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were 10 recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 15 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhMapper.pl>) to determine the 20 probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

25

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

30

CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;
- (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and
- 15 (c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing 25 polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein
5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413,
10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a
15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396,
20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one
25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530,
30 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111,
5 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-
225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390,
392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-
444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

10 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

15 10. A host cell transformed or transfected with an expression vector according to claim 9.

20 11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-
25 160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225,
227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392,
393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444,
446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

30

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.

5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

10 14. A fusion protein comprising at least one polypeptide according to claim 1.

15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

15

16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

20 17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.

18. An isolated polynucleotide encoding a fusion protein according to claim 14.

25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to any one of claims 11-13;
- (d) a fusion protein according to claim 14; and

30

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;
(b) a polynucleotide according to claim 4;
(c) an antibody according to any one of claims 11-13;
(d) a fusion protein according to claim 14; and
(e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant 15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.

29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.

10

30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.

31. A method for inhibiting the development of a cancer in a patient, 15 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.

20

32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.

33. A method according to any one of claims 23, 24 and 31, wherein the 25 cancer is prostate cancer.

34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is 30 encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5 wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35. A method according to claim 34, wherein the biological sample is
10 blood or a fraction thereof.

36. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15 37. A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;
20 (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
25 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
(iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),
under conditions and for a time sufficient to permit the stimulation and/or
expansion of T cells.

38. An isolated T cell population, comprising T cells prepared according to the method of claim 37.

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

10 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

15 (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20 41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

25 (i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i)
or (ii);

such that T cells proliferate;

- (b) cloning at least one proliferated cell to provide cloned T cells; and
5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111,
15 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

20 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

- 25 44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate
30 cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- 15 (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

25

49. A method according to claim 46, wherein the cancer is a prostate

cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

20

53. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5 54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

10 55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

15 56. A diagnostic kit, comprising:
(a) one or more antibodies according to claim 11; and
(b) a detection reagent comprising a reporter group.

57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20 58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

25 59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171,
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5 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any
of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the
oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO:
10 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-
111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220,
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442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

15

62. A diagnostic kit, comprising:
(a) an oligonucleotide according to claim 61; and
(b) a diagnostic reagent for use in a polymerase chain reaction or
hybridization assay.

20

63. A host cell according to claim 10, wherein the cell is selected from
the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim
25 10.

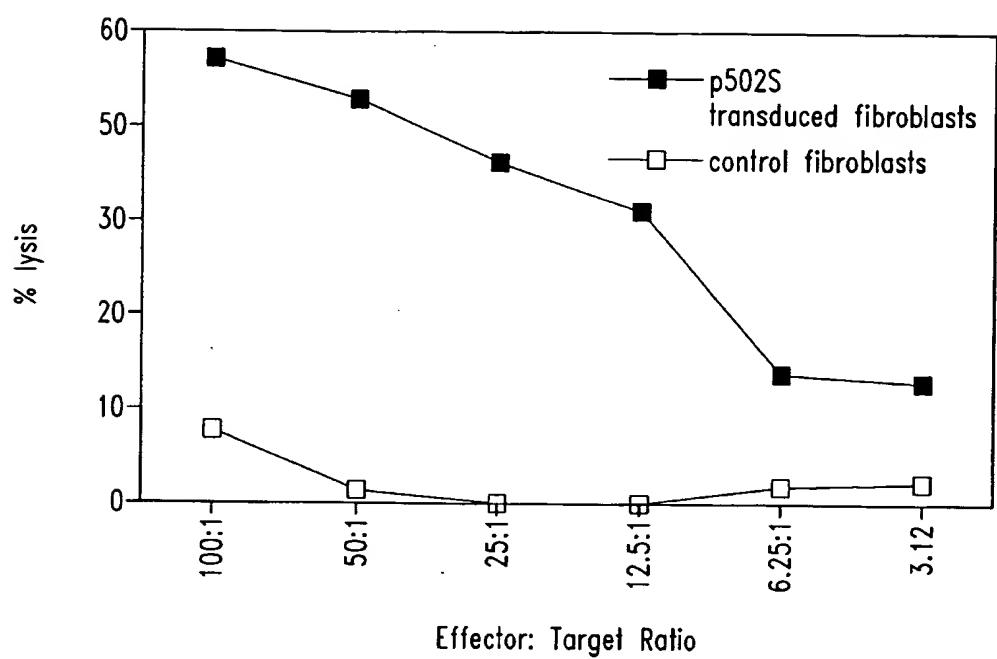


Fig. 1

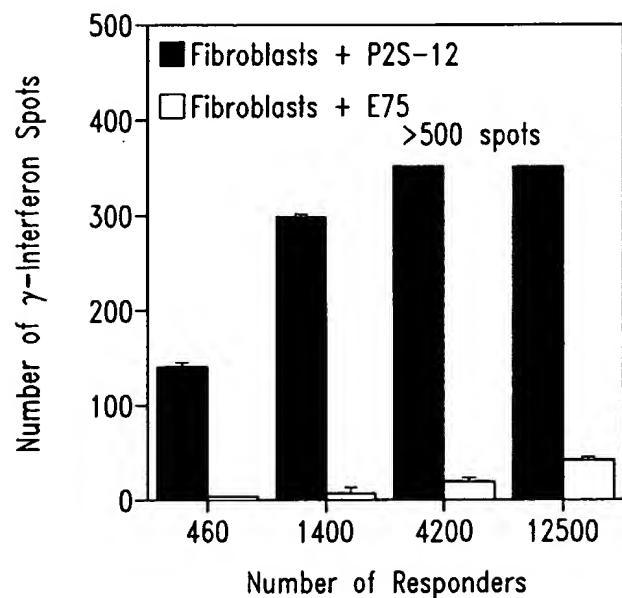


Fig. 2A

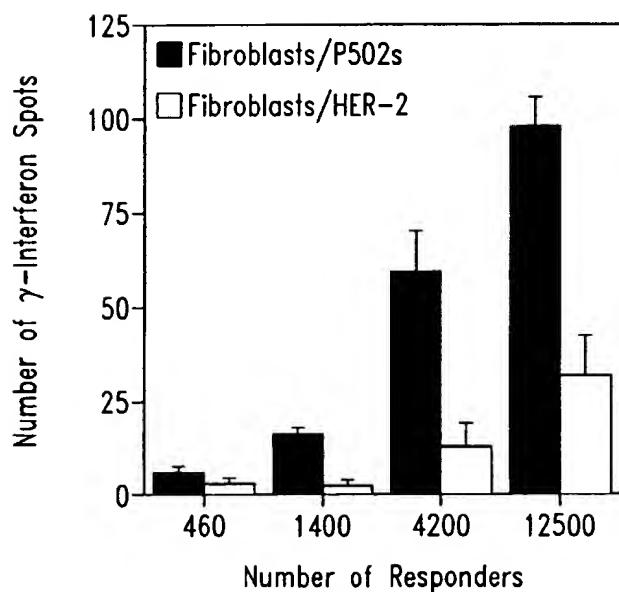


Fig. 2B

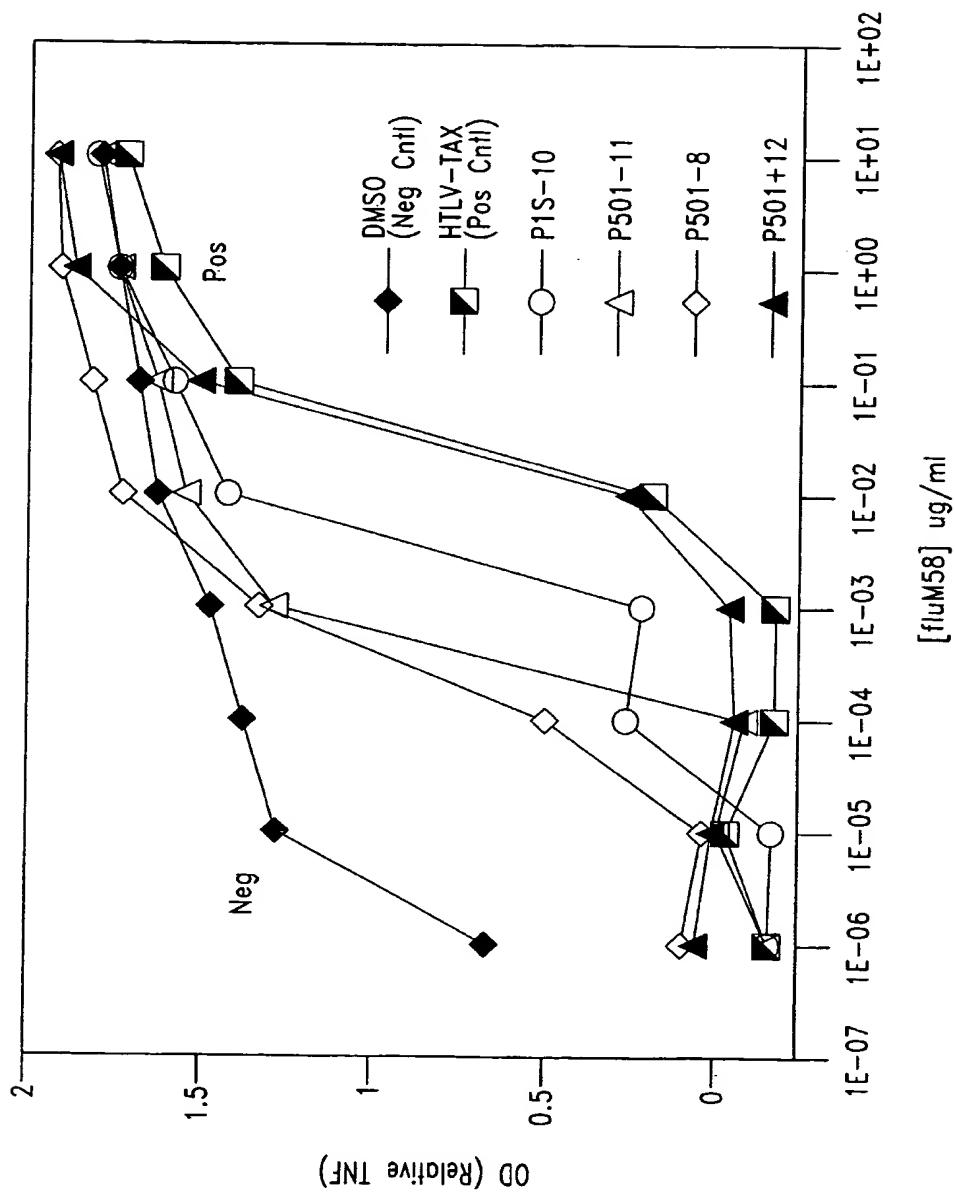


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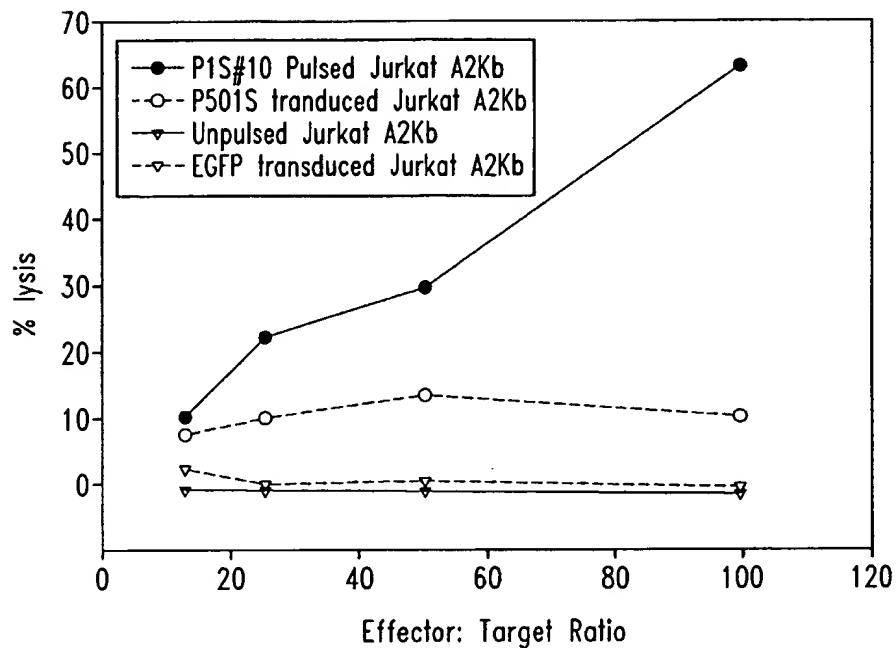


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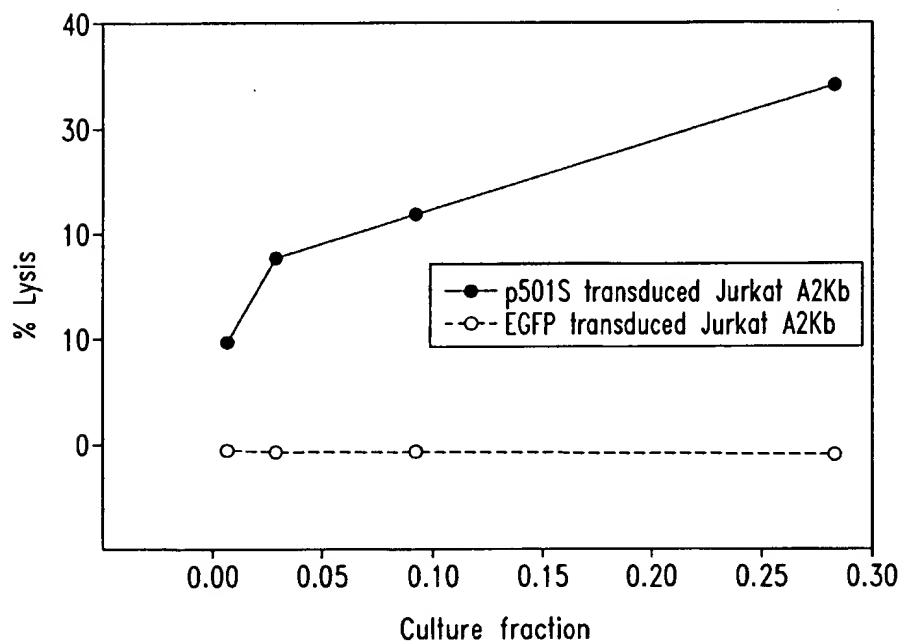


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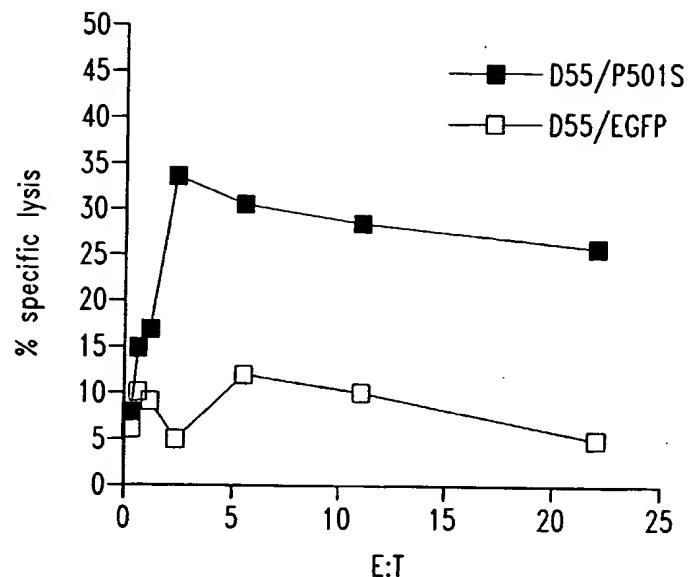


Fig. 6A

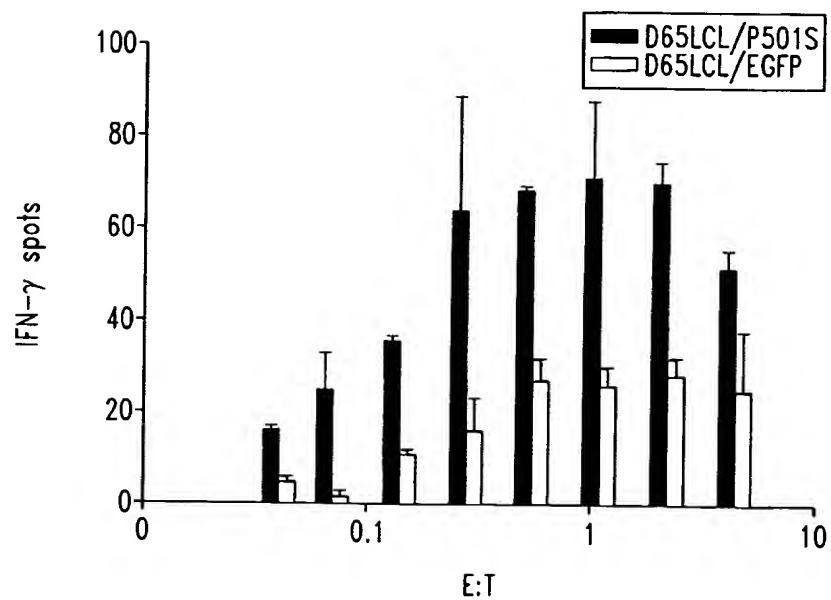
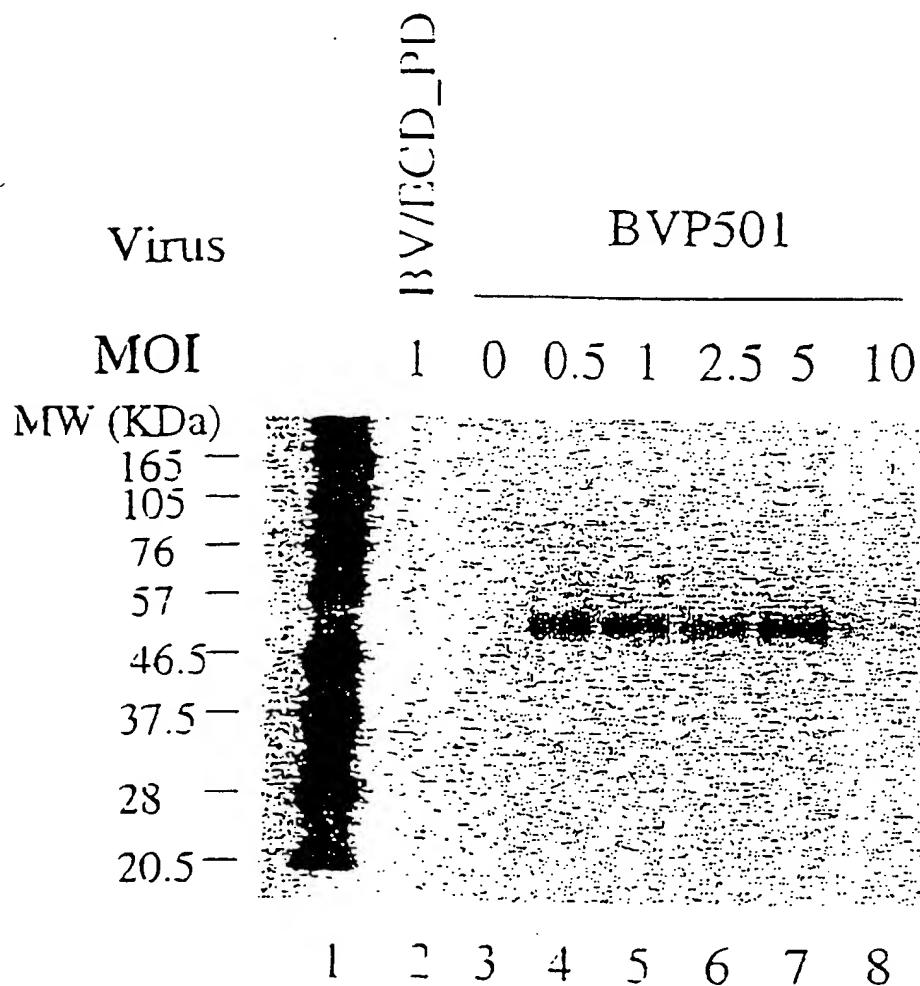


Fig. 6B

Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 8-well plate were infected with an unrelated control virus BV/ECD_PD (lane 1), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against F⁺1S (F501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (Sigma).

Fig. 7

**Figure 8. Mapping of the epitope recognized by
10E3-G4-D3**

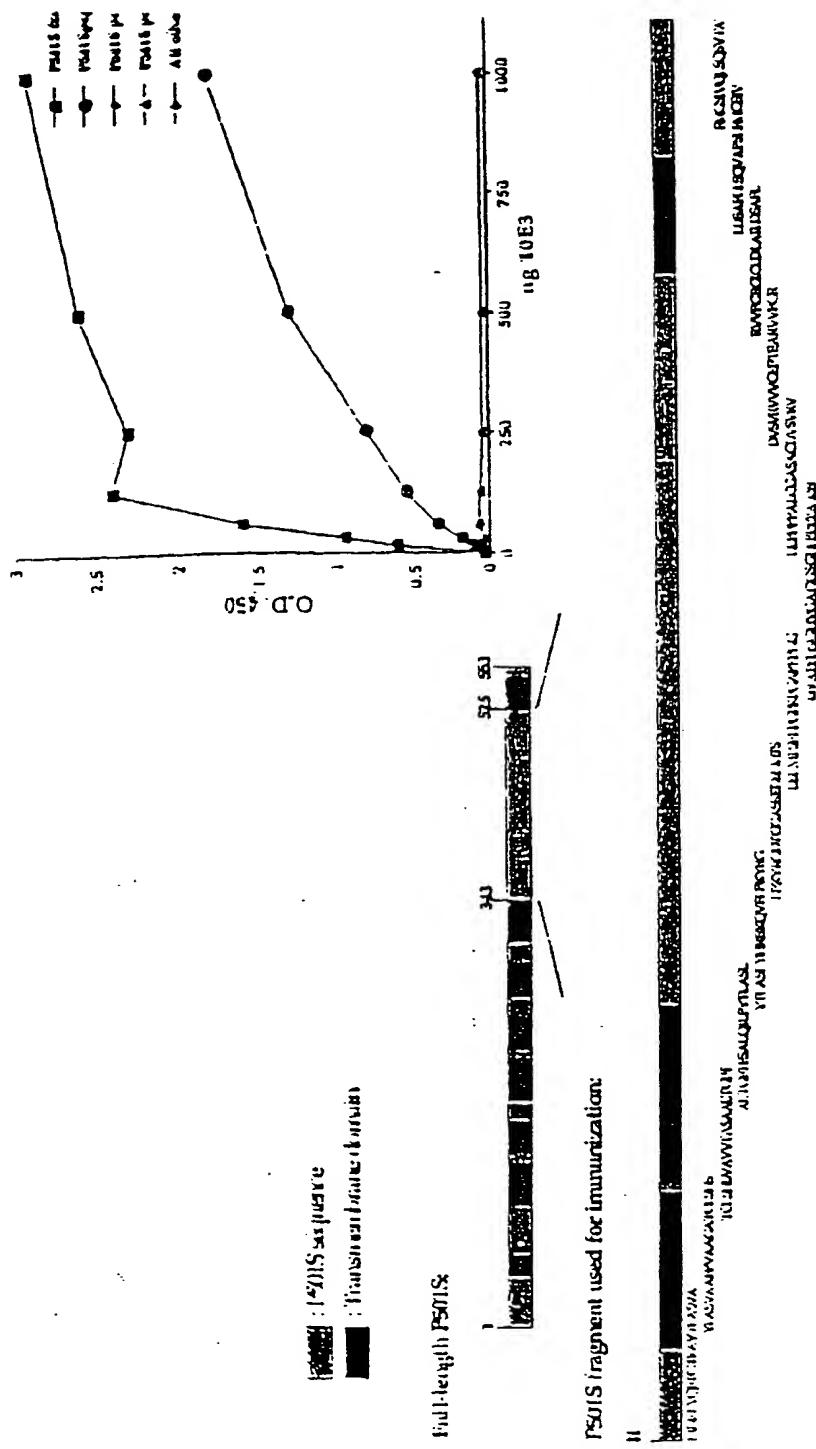


Fig. 8

Schematic of P501S with predicted
transmembrane, cytoplasmic, and extracellular regions

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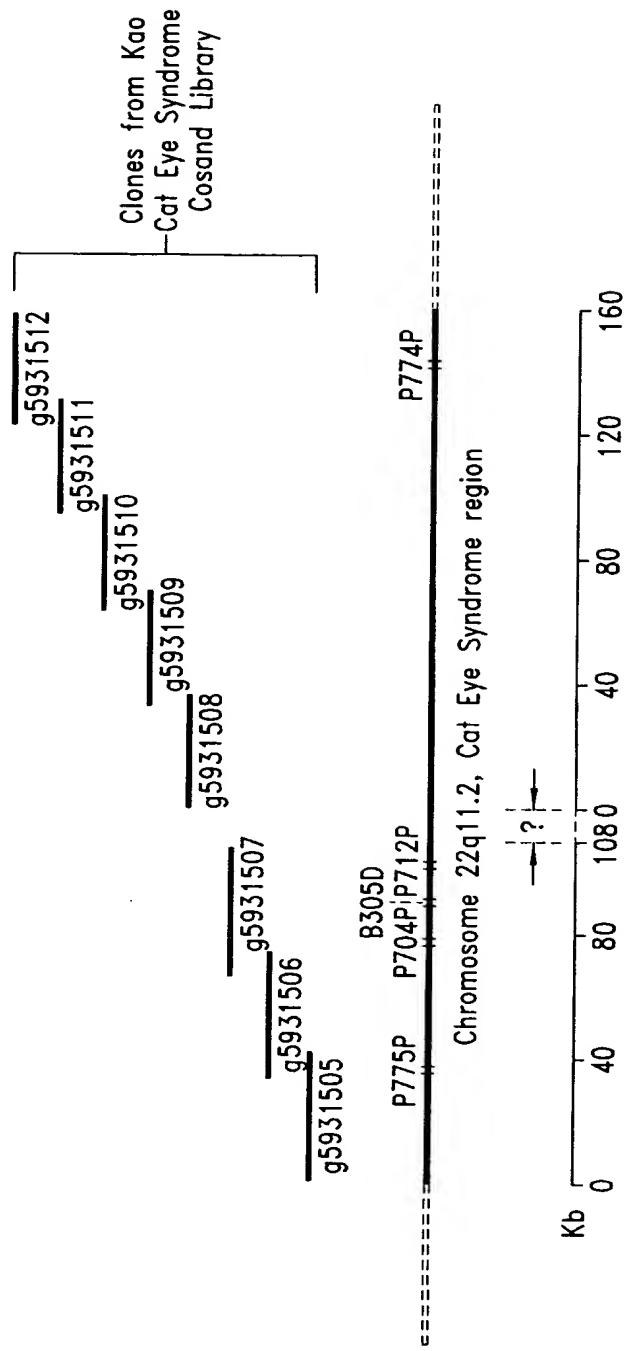
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Underlined sequence: Predicted transmembrane domain; **Bold sequence**: Predicted extracellular domain; *Italic sequence*: Predicted intracellular domain. Sequence in bold/underlined: used generate polyclonal rabbit serum

Localization of domains predicted using HMMTOP (G.E. Tusnady an I. Simon (1998) Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to topology Prediction. J.Mol Biol. 283, 489-506.

Fig. 9

*Fig. 10*

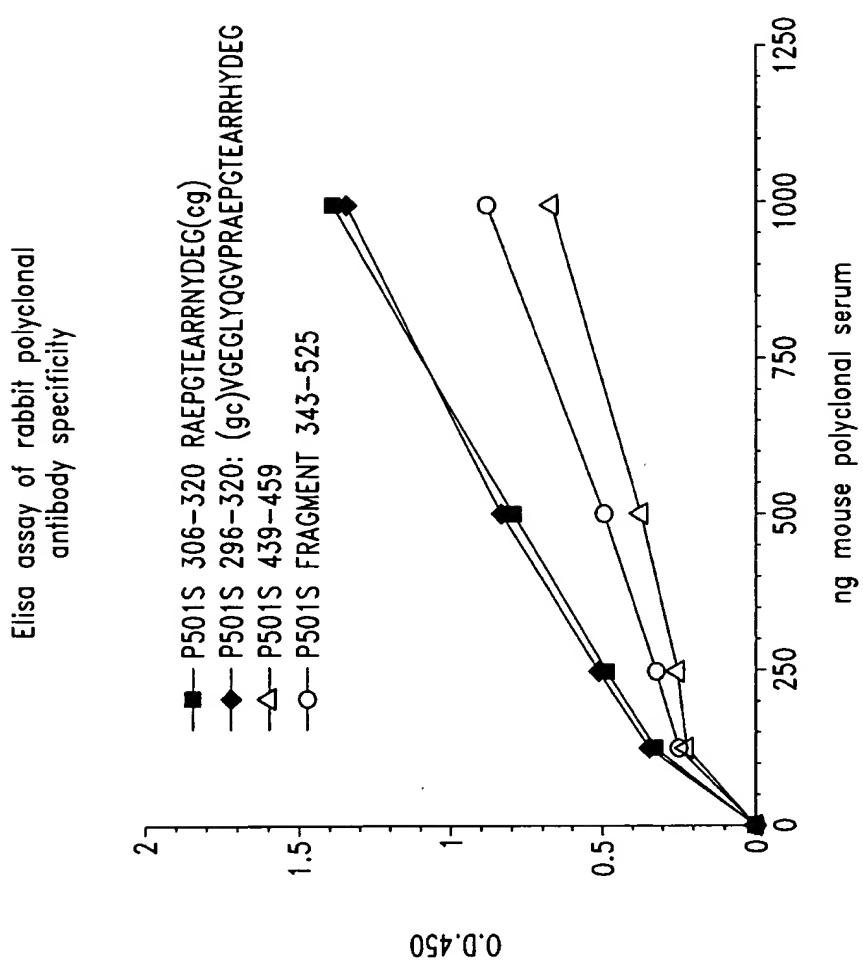


Fig. 11

SEQUENCE LISTING

<110> Corixa Corporation
 Xu, Jiangchun
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 Mitcham, Jennifer L.
 Harlocker, Susan Louise
 Jiang Yuqui
 Reed, Steven G.
 Kalos, Michael
 Fanger, Gary
 Retter, Mark
 Solk, John
 Day, Craig
 Skeiky, Yasir A.W.
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<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND
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<223> n = A,T,C or G
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<400> 7

tttttttttt	tttttttttt	tggctctaga	gggggttagag	gggggtctat	agggttaaata	60
cggggccctat	ttcaaaagatt	tttaggggaa	ttaattctag	gacgtatgggt	atgaaaactgt	120
ggtttgcgcc	acagatttca	gagcattgac	cgtatgtatac	ccccgggtcg	gtagcgggtga	180
aagtggtttg	gttttagacgt	ccgggaattt	catctgtttt	taagcctaatt	gtggggacag	240
ctcatgagtg	caagacgtct	tgtgatgtaa	ttattatacn	aatgggggt	tcaatcgga	300
gtactactcg	attgtcaacg	tcaaggagtc	gcagggtcgcc	tggttctagg	aataatgggg	360
gaagtatgtt	ggaattgaag	attaatccgc	cgtatcggt	gttctcttag	gttcaataacc	420
attggtgccc	aattgatttt	atggtaaggg	gagggtatcg	tgaactcgtc	tgttatgtaa	480
aggatncctt	ngggatggga	aggcnatnaa	ggactangga	ttaatggcg	gcangatatt	540
tcaaacngtc	tctanttcct	gaaacgtctg	aaatgttaat	anaattaan	tttnngttatt	600
gaatnttnng	gaaaagggt	tacaggacta	gaaacccaat	angaaaanta	atnntaangg	660
crrttatcntr	aaaggttnata	accnctccct	tnatcccacc	caatngnatt	ccccacncnn	720
acnattggat	nccccanttc	canaaanggc	cnccccccgg	tgnannccnc	cttttgttcc	780
cttnantgan	ggttattcnc	ccctngcnnt	atcanc			817

<210> 8
<211> 799
<212> DNA
<213> *Homo sapien*

```
<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A, T, C or G
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<400> 8

cattttccccgg	tttactttct	aaggaaagcc	gagcggaaagc	tgctaacctg	ggaatcggt	60
cataaggaga	actttctgt	ggcacgcgt	agggacaagc	gggagagcga	ctccgagcgt	120
ctgaagcgc	cgtcccagaa	ggtggactt	gcactgaaac	agctgggaca	catccgcag	180
tacgaacacg	gcctgaaa	agt gctggagcgg	gagg	ttccagc	agtgttagccg	240
tgggtggccg	angcctganc	cgctctgc	tgctgc	ccccccccc	angtgggccc	300
acctgcctgg	gtccaaacac	tgagccctgc	tgccggactt	caaggan	ccccacangg	360
ggatttgt	cctanantaa	ggctcatct	ggcctcg	cccccac	ctg gttggc	420
tctttgangt	gagccccat	g tccatct	ccactgt	tcng	gaccac	480
ctccttacaa	ccacannat	g cccggct	cccg	ggaaacc	antcccancc	540
caagncc	atccactnnt	nctanaacc	gcnc	ccncc	cngtggaaacc	600
tcctttc	ntnaggttaa	tnncgc	tc	ttncan	ngtctncn	660

gttnaaattg ttangcccc nccnntccn cnncnnnan cccgaccnn annnnann ncctgggggt nccnnngat tgacccnncc nccctntant tgcntnggg nnccntgcc cttccctct ngganncg	720 780 799
<210> 9	
<211> 801	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(801)	
<223> n = A,T,C or G	
<400> 9	
acgccttgat cttcccaggc tggactgg tctggagga gcccgcatt ctgtggttt taangatgac actcccaaag gtggcttga cagtggccca gatggacatg gggctcacct caaggacaag gccaccaggc gcggggcccg aagccacat gatecttact ctatgagcaa aatccccgtt gggggcttct cttgaagtc cgccancagg gtcagtctt tggacccang caggcatgg gttgtngnc caactgggg ccncaacgca aaanggcna gggctcnng caccatccc angacgcgc tacactnctg gaccccncn tccaccaett tcatgcgcgt ttcntaccc cgnatntgtc ccanctgtt cngtgcnnac tccanettct nggacgtgcg ctacatacgc cggantcnc nctcccgctt tgccctatc cacgtncan caacaaattt cnccntantg caccnattcc acncttnnc agntttccnc nnccngcttc cttntaaaag ggttganccc cggaaaatnc cccaaagggg gggggccngg taccctaactn cccctnata gctgaantcc ccatnacnn gnctcнатtgg anccntcent tttaaannacn ttctnaactt ggaaananc ctcgnccn ccccnntaa tcccnccctt cngnncnt ccccnntcc nccnnntng gcnttnann cnaaaaaggc ccnnnacaa tctcnnncn ctcanttcg ccanccctcg aaatcgccn c	60 120 180 240 300 360 420 480 540 600 660 720 780 801
<210> 10	
<211> 789	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(789)	
<223> n = A,T,C or G	
<400> 10	
cagtctatnt ggccagtgtg gcagcttcc ctgtggctgc cgggccaca tgctgtccc acagtgtggc cgtggtaaca gttcagccg ccctcaccgg gttcaccttc tcagccctgc agatctgccc tctacacactg gctccctct accacccggga gaagcagggtg ttccctgccc aataccgagg ggacactgga ggtgttagca gtgaggacag cctgtatgacc agtttctgc caggccctaa gcctggagct ccctcccta atggacacgt ggggtcttga ggcagtggcc tgctccctacc tccacccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg tgggggtga gcccaccgan gcccagggtgg ttccggccgg gggcatctgc ctggacccctcg ccatcttggta tagtgccttcc tgctgtccc ngtggccca tccctgttta tgggtctccat tgtccagctc agccagtctg tcactgccta tatgggtct gcccggcc tgggtctgg cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg ttaaaaattt ccagcaacat tgggggtga aggcctgcct cactgggtcc aactccccgc tcctgttaac cccatggggc tgccggcttgc gcccacatt tctgttgcgtt ccaaantnat gtggctctct gtcgtccacctt gttgtggctt gaagtgcnta cngcncanct ngggggtng ggngtcccc	60 120 180 240 300 360 420 480 540 600 660 720 780 789
<210> 11	
<211> 772	

```

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (772)
<223> n = A,T,C or G

<400> 11
cccacccctac ccaaataat gacaccaaca cagaaaaagct agcaatggat tcccttctac      60
tttgttaat aaataagtt aatattaaa tgctgtgtc tctgtatgg caacagaagg      120
accaacaggc cacatcctga taaaaggtaa gaggggggggtg gatcagcaaa aagacagtgc      180
tgtgggctga ggggacctgg ttcttggtg ttgccccctca ggactcttcc cctacaaaata      240
actttcatat gttcaaatcc catggaggag ttttcattcc tagaaactcc catgcaagag      300
ctacattaaa cgaagctgca ggttaagggg ctanagatg gaaaaccagg tgactgagtt      360
tattcagctc ccaaaaaccc ttctcttaggt gtgtctcaac taggaggcta gctgttaacc      420
ctgagcctgg gtaatccacc tgcagagtcc cccatccca gtgcattggaa cccttctggc      480
ctccctgtat aagtccagac taaaaccccc ttgaaaggnc tccagtcagg cagccctana      540
aactgggaa aaaagaaaaag gacgccccan ccccccagctg tgcancatcg cacctcaaca      600
gcacagggtg gcagaaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca      660
acccggcac cccnanggg gttacagga ancngggnaa ctttggcacc aattnaggca      720
ggcccnccac cccnaatntt gctggaaat ttttccccc ctaaattntt tc      772

<210> 12
<211> 751
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (751)
<223> n = A,T,C or G

<400> 12
gcccccaattc cagctgccac accacccacg gtgactgcat tagttcgat gtcataaaaa      60
agctgattga agcaacccctc tactttttgg tcgtgagcct ttgtctggc gcaagggttca      120
ttggctgtgt tggtgacgtt gtcattgcaaa cagaatgggg gaaaggcact ttctcttttgc      180
aagtanggtg agtcctcaaa atccgtatag ttgtgtgaagc cacagcaactt gaggcccttc      240
atgggtgtgt tccacactt agtgaagtct tcctgggaaac cataatctt ctgtatggca      300
ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac      360
agcagctgc acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc      420
acacttgc tcaatctt caccatanca gcccgtggaa accaananca aagaccacna      480
cnccggctgc gatgaagaaa tnacccncg ttgacaaaact tgcacccac tggganccac      540
agtggccna aaaatcttca aaaagatgc cccatcnatt gaccccccatt atgcccactg      600
ccaacagggg ctgccccacn cnccnaacga tgancnatt gnacaagatc tnctggct      660
tnatnaacnt gaaccctgcn tngtgctcc ttttcaggnc cnnggctga cttctnaann      720
aangaactcn gaagnccca cngganann g      751

<210> 13
<211> 729
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (729)
<223> n = A,T,C or G

```

<400> 13

gagccaggcg tccctctgcc	tgcccactca	gtggcaaacac	ccgggagctg	ttttgtcctt	60
tgtggancct cagcagtnc	ctcttcaga	actcantgcc	aagancctg	aacaggagcc	120
accatgcagt gcttcagett	cattaagacc	atgatgatcc	tcttcattt	gctcatcttt	180
ctgtgtggtg cagccctgtt	ggcagtggc	atctgggtgt	caatcgatgg	ggcattctt	240
ctgaagatct tcgggcaact	gtcgccagt	gccatgcagt	ttgtcaacgt	ggctacttc	300
ctcatcgca	ccggcggtgt	ggtcttagct	ctaggttcc	tgggctgcta	360
actgagagca agtgtgcct	cgtgacgttc	ttcttcatcc	tcctccat	cttcattgtct	420
gaggttgcaa tgctgtggtc	gccttgggt	acaccacaat	ggctgagcac	ttcctgacgt	480
tgctggtaat gcctgccc	ataaaaagat	tatgggttcc	caggaanact	tcaactcaagt	540
gttggAACAC caccatggaa	gggctcaagt	gctgtggctt	cnnccaacta	tacggatttt	600
gaagantcac ctacttcaaa	gaaaanagtg	ccttcccccc	atttctgtt	caattgacaa	660
acgtccccaa cacagccaat	tgaaaacctg	cacccaaccc	aaangggtcc	ccaaccanaa	720
attnaaggg					729

<210> 14

<211> 816

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(816)

<223> n = A,T,C or G

<400> 14

tgctcttcct caaagggttt	cttgggtgcca	taacaaccac	cataggtaaa	gcgggcgcag	60
tgttcgctga aggggttgta	gtaccagcgc	gggatgctct	ccttgcagag	tcctgtgtct	120
ggcaggcaca cgcagtgc	tttgcactg	ggggaaatgga	tgcgctggag	ctcgctcaaag	180
ccactcgtgt attttcaca	ggcagcctcg	tccgacgcgt	cggggcagtt	gggggtgtct	240
tcacactcaca ggaaactgtc	natgcagcg	ccattgtctgc	agcggaaatgc	gggtggctga	300
cangtgcac	agcacactgg	atggcgcctt	tccatgnnan	gggccttgng	360
tgancccccan	anctgcctt	caaangcccc	accttgacaca	ccccgacagg	420
atcttcttcc	cggaaaggtag	ttntttctgt	tgcggcaancc	ancccnntaa	480
gcanatctgc	tccgnggggg	tcttantacc	anctgtggaa	aagaacccca	540
caancttgc	tggatnccaa	gcnataatct	ncnttctgc	ggcngcgaac	600
ctgtnnanct	ttagnccntg	gtcctcntgg	gttgnncttg	aacctaatcn	660
gggacaaggt	aanntngccnt	cctttnaatt	ccnancntr	ccccctgggtt	720
cncnctctca	ccccagaaaan	nccgttcc	cccccaacta	ggggccnnaaa	780
cacaaccctn	ccccaccac	gggttcngnt	ggttng	ccnnttnttc	816

<210> 15

<211> 783

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(783)

<223> n = A,T,C or G

<400> 15

ccaaggcctg ggcaggcata	nacttgaagg	tacaacccca	ggaacccctg	gtgctgaagg	60
atgtggaaaa	cacagattgg	cgcctactgc	ggggtgacac	ggatgtcagg	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaaang	cacctacctg	180
cagtactag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtca	240
ccaagcagac	agaagactac	tgcctcgcat	ccaaacaangt	gtgctgtcca	300
tcccacgctg	gtactatgac	cccacggagc	agatctgcaa	gggtcgctgc	360
				gagtttcgtt	tatggaggct

gcttggcaa caagaacaac tacttcggg aagaagagtg cattctanc	tgtcnnggtg	420
tgcaaggta gccttgana ngcancatcg gggctcangc gactttccc	caggccccct	480
ccatggaaag ggcacatcca ntgttctcg gcacctgtca gcccacccag	ttccgctgca	540
ncaatggctg ctgcacnac antttctng aattgtgaca acaccccca	ntgccccaa	600
ccctcccaac aaagttccc tttttaaaa tacnccantt ggcttttnac	aaacccccgg	660
cncctccnntt ttecccnntn aacaaggc nctngcnntt gaactgccc	aaccnngaa	720
tctnccnngg aaaaantncc cccctgggtt cctnnaancc ctcnccnaa	anctncccc	780
ccc		783
<210> 16		
<211> 801		
<212> DNA		
<213> Homo sapien		
<220>		
<221> misc_feature		
<222> (1)...(801)		
<223> n = A,T,C or G		
<400> 16		
gccccaaattc cagctgccac accacccacg gtgactgcat tagttcgat	gtcataaaaa	60
agctgattga agcaaccctc tactttttgg tcgtgagccct tttgcttgt	gcaggttca	120
ttggctgtgt ttgtgacgtt gtcattgcaa cagaatgggg gaaaggact	gttcttttg	180
aagttaggtg agtcctcaaa atccgtatag ttgtgaaagc cacagcactt	gagcccttc	240
atgggtgtgt tccacacttg agtgaagtct tcctggaaac cataatctt	cttgatggca	300
ggcaactacca gcaacgtca gaaatgtca gocattgtgg tgtacaccaa	gggaccacaca	360
gcagctgcaa ccttagcaat gaagatgagg aggaggatga agaagaacgt	cncgagggca	420
cactgtctt ccgtcttagc accatagcag cccangaaac caagacaaa	gaccacaacg	480
ccngctgcga atgaaagaaa ntacccacgt tgacaaactg catggccact	ggacgacagt	540
tggcccgaan atcttcagaa aaggatgcc ccattgattt aacacccana	tgcccactgc	600
cnacaggcgt genccenncn gaaagaatga gccattgaag aaggatcntc	ntgtcttaa	660
tgaactgaaa ccttgcattt tggccctgt tcagggtctt tggcagtgaa	ttctganaaa	720
aaggaacngc ntnagcccc ccaaangana aaacacccccc ggggtttgcc	ctgaattggc	780
ggcaaggan ccctgccccn g		801
<210> 17		
<211> 740		
<212> DNA		
<213> Homo sapien		
<220>		
<221> misc_feature		
<222> (1)...(740)		
<223> n = A,T,C or G		
<400> 17		
gtgagagcca ggcgtccctc tgcctgccc ctcagtggca acacccggga	gctgttttgt	60
ccttggaa gcctcagcag ttccctttt cagaactcac tgccaagagc	cctgaacagg	120
agccaccatg cagtgttca gtttattaa gaccatgatg atccctttca	atttgctcat	180
ctttctgtgt ggtcagccc ttgtggcagt gggcatctgg gtgtcaatcg	atggggcatc	240
ctttctgaag atttcgggg cactgtcgcc cagtgtccatg cagtttgtca	acgtgggcta	300
cttccttcatc gcagccggcg ttgtggctt tgcttttgtt tcctgggct	gctatggtgc	360
taagacggag agcaagtgtt ccctcgatc gtcttttttcc atcccttcc	tcatcttcat	420
tgctgaagtt gcaatgtgtt ttgtggcattt ggtgtacacc acaatggctg	aaccattctt	480
gacgttgcgt gtatgtccatg ccatcaanaa agattatggg ttcccaaggaa	aaatttactc	540
aatntggaa cacccnccatg aaaaggcgtt caatttctgn tggcttcccc	aactataccg	600
gaattttgaa agantcnccc tactttccaaa aaaaaanant tgcctttncc	ccctttctgt	660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnncaaaaaa	gnntcncaa	720

caaaaaaaant nnaagggttn	740
<210> 18	
<211> 802	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(802)	
<223> n = A,T,C or G	
<400> 18	
ccgctggttg cgctggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca	60
caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcataatg	120
ggatacactt tacttttagca gccagggtga caactgagag gtgtcgaaagc ttattttct	180
gaggctctgt tagtggagga agattccggg cttcagctaa gtatcgatcg tatgtccccat	240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa	300
cattggcat gtccagcagt tctccaaaca cgtagacacc agnngcctcc agcacctgat	360
ggatgagtgt ggccagcgtt gcccccttgg ccgacttggc taggaggaga aattgtctct	420
ggttctgccc tgtaaccccttc acttccgcac tcatcactgc actgagtgtag ggggacttgg	480
gctcaggatg tccagagacg tggccggcc ccctcnnta atgacaccgn ccanmcaacc	540
gtccggctccc gcccgttng ttcgtcgtncc ctgggtcagg gtctcgatgg cnctacttgc	600
aancttcgtc nggcccatgg aatttacccnc accggaaactn gtangatcca ctnnttctat	660
aaccggncgc caccgnntt ggaatccac tcttnttncc tttacttgag ggttaaggtc	720
accctnnncg ttaccttggt ccaaacntn ccntgtgtcg anatngtnaa tcnggnccna	780
tncancancnc atangaagcc ng	802
<210> 19	
<211> 731.	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(731)	
<223> n = A,T,C or G	
<400> 19	
cnaagcttcc aggttacggg ccgcnancc tgacccnagg tancanaang cagnncngcg	60
gagcccaccc tcacgngng gngtctttat nggagggggc ggagccacat cnctggacnt	120
cntgacccca actcccccnc ncncantgca gtatcgatgt cagaactgaa ggttacgtgg	180
caggaaccaa gancaaannc tgctccnnnt caagtccggcn naggggccgg ggctggccac	240
gcncatccnt cnagtgtctgn aaagcccccnn ctgtctact tggggagaa acngcnngna	300
catgcccagn gttanataac nggcngagag tnantttgcc tctcccttcc ggctgcecan	360
cgngtntgct tagnggacat aacctgacta cttactgaa cccnngaate tnccnccct	420
ccactaagct cagaacaaaaa aacctcgaca ccactcantt gtcacctgnc tgctcaagta	480
aagtgtaccc catncccaat gtntgctng a ngtctgncc tgcnttangt tcggctctgg	540
gaagacctat caattnaagc tatgtttctg actgcctt gctccctgna acaanncnacc	600
cnnccnntcca aggggggggncc ggcccccataat ccccccacc ntnaattnan ttancccn	660
cccccnngcc cggccctttta cnancntcnn nnacnnggna aaacccnnngc ttncccaac	720
nnaatccncc t	731
<210> 20	
<211> 754	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(754)
<223> n = A,T,C or G

<400> 20
.tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaattgtc      60
caacccttc ntccaaatnn ccnttccgg gnggggggttc caaacccaa ttannttgg      120
annttaaatt aaatntnnt tggnngnnna anccnaatgt nangaaagtt naacccanta      180
tnancttnaa tncctggaaa ccngtngntt cccaaaatnt ttaaccctta antccctcg      240
aaatngtta nggaaaaccc aanttctcnt aagggtgtt gaaggntnaa tnaaaanccc      300
nnccaattgt tttngccac gcctgaatta attggnntcc gntgtnncc nttaaaanana      360
ggnnanccccc gtttantha tcccccnnc cccaattata ccgantttt ttngaattgg      420
ganccncgg gaattaaacgg ggnnnntccc tnttgggggg cnggnncccc cccntcggg      480
ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc      540
ccaggnctgag nntngggttt ncccccccc cangggccct ctgcnanagt tggggttgg      600
ggggcctggg attttnttcc ccctnttnc tcccccccccc cengganag aggttngngt      660
tttgntcnc ggcncncn aagancttn ccganttnan ttaaatccnt gcctnggcga      720
agtccnttgn agggntaaan ggcccccnnn cggg                                754

<210> 21
<211> 755
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(755)
<223> n = A,T,C or G

<400> 21
atcancccat gacccnaac nngggaccnc tcancggnc nnncnaccnc cggccnatca      60
nngtnagnnc actncnntt natcacnccc cnccnactac gcccnchanc cnacgncta      120
nnccanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccaanacn      180
ccagctgtcc nanaangccct nnnatacngg nnnatccaat ntgnancctc cnaagtattn      240
nnccnccanat gatttcctn anccgattac ccntnccccc tanccctcc cccccaacna      300
cgaaggcnct gnccnaagg nngcgncc cccctagntc cccncaagt cnccncccta      360
aactcancn nattacnccgc ttentgagta tcaactccccg aatctcaccc tactcaactc      420
aaaaanatcn gataaaaaat aatncaagcc tgnttatnac actntgaactg ggtctctatt      480
ttagnggtcc nttaancntc ctaatacttc cagtctnct tcnccaattt ccnaanggct      540
ctttcngaca gcatntttt gttcccnntt gggttcttan ngaattgccc ttcntngaac      600
gggctctct ttcccttcgg ttancttgnn ttccnccggc cagtttat ttcccnntt      660
aaatttentnc ntttanttt tggcmttca aaaaaaaaaa cttgaaaacg gccccctgg      720
aaaaggttgt ttganaaaaa tttttgtttt gtcc                                755

<210> 22
<211> 849
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(849)
<223> n = A,T,C or G

<400> 22
tttttttttt tttttangtg tngtcgtgca ggttagaggct tactacaant gtgaanacgt      60
acgctnggan taangcgacc cganttctag gannccctt aaaatcanac tgtgaagatn      120

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atcctgnnna	cggaangtc	accggnnngat	nntgctaggg	tgnccnctcc	cannncnttn	180
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tctgtcttcc	cctgnagncn	anaaantggg	ccnccgnccc	ctttacccct	nnacaaggcca	360
cngccntcta	nccncngccc	ccccctccant	nngggggact	gcenannget	ccgttnctng	420
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cncnegrnng	cctcnccctcg	caacacccgc	ntctntengt	ncggnnnnccc	ccccacccgc	600
ncctcncnc	ngncgnancn	ctccnccncc	gtctcanmca	ccaccccgcc	ccgcccagggcc	660
ntcancacn	ggnngacnng	nagncnnntc	genccgccc	gcnncnccct	cgccncngaa	720
ctncntcngg	ccanrnncgc	tcaanccnna	cnaaacgccc	ctgcgcggcc	cgnagcgncc	780
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nncangcgg						849

<210> 23
<211> 872
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(872)
<223> n = A,T,C or G

<400> 23

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cacacncnan	aganaaatcc	netgccttc	anagtanacn	attgaacnng	agaaccangc	180
ngcgaatcg	taatnagggc	tgcgcgc	atntgtcncc	gtttattnn	ccagcncnc	240
ctnccnaccc	tacntctcn	nagctgtcn	accctngt	cgnacccccc	naggtcg	300
tcgggtttn	nntgaccng	cnncctcc	ccccntccat	nacgancenc	ccgaccacc	360
nanngcncgc	ncccgcnct	cttcgcnncc	ctgtcctn	ccccgtngc	ctggcncngn	420
accgcattga	ccctegccnn	ctncnngaaa	ncgnanacgt	ccgggtgnn	annancgctg	480
tgggnnngcg	tctgencgc	gttccttccn	ncnmcttcca	ccatcttnt	tacnggtct	540
ccnccgc	tcnnncacn	cctggacgc	tntcctntgc	cccccttnac	tccccccctt	600
cgnegtgnc	cgnccccacc	ntcatttca	nacgmttcc	acaannncct	ggntnnctcc	660
cnancngncn	gtcanccnag	ggaagggng	ggmccnnntg	nttgcgttg	nggangtgc	720
cgaanantcc	tcnccntcan	cnctacccct	cgggcgnct	ctcngtnc	aacttancaa	780
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<210> 24
<211> 815
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(815)
<223> n = A,T,C or G

<400> 24

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tcntncatta	gtaacaantg	tnntgtccat	cctgtcngan	canattccca	ttnattncgn	180
cgcattcn	gcncantatn	taatnnggaa	ntcnnntnnn	ncacccnncat	ctatcntcc	240
gcncctgac	tggnagagat	ggatnanc	tnntntgacc	nacatgtca	tcttgattn	300
aananc	cgcnccac	cggttngnng	cnagccnn	ccaagaccc	ctgtggaggt	360

aacctgcgtc aganncatca aacntggaa acccgcncc angtnnaagt ngnnnccan	420
gatcccgtcc aggnntnacc atcccttcnc agcgccccct ttngtgcctt anagngnagc	480
gtgtccnanc cnctcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc	540
gaacccctta gggggantna tncaaanccc caggattgtc cncncangaa atcccncanc	600
cccncctac cnnncttgg gacngtgacc aantcccgga gtnccagtcc ggcgnctc	660
ccccacccgt nnccntgggg gggtaanct cngnntcanc cngncgaggn ntcgnaagga	720
accggnctn ggnngaann ancnntcnga agngccncnt cgtataaccc cccctcncca	780
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<210> 25	
<211> 775	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(775)	
<223> n = A,T,C or G	
<400> 25	
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agtcaaattt cctgaatttc tatgtgtctg ggtttcatcc atccgacatt gaanttgact	180
tactgaagaa tgganagaga attgaaaaag tggagcatc agacttgtct ttcaagcaagg	240
actggctttt ctatctcnng tactacactg aattcacccc cactgaaaaa gatgagttatg	300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca	360
tgttaagcagn cnncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt	420
ctgcttgcctt gcntttaat antgatatgc ntatacaccc taccctttat gnccccaat	480
tgttaggggtt acatnантgt tcncntngga catgatctc ctttataant ccncnttcg	540
aattggccgt cncccnngtn ngaatgttcc cnnaaccacg gttggctccc ccaggtcncc	600
tcttacggaa gggcctggc cncttncaa ggttggggga accnaaaatt tcnctntgc	660
ccncccncca cnntcttng nncncanttt ggaacccttc cnattccct tggctcnna	720
ncctnncta anaaaactn aaancgtng naaanntttt acttcccccc ttacc	775
<210> 26	
<211> 820	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(820)	
<223> n = A,T,C or G	
<400> 26	
anattantac agtgtatct tttccagag gtgtgtanag ggaacggggc ctagaggcat	60
cccanagata ncttatanca acagtgtttt gaccaagagc tgctggcac atttcctgca	120
gaaaaggtgg cgggtcccat cactcctctt ctcccatagc catcccagag gggtagtag	180
ccatcangcc ttcgggtggg gggagtcang gaaacaacan accacagagc anacagacca	240
ntgatgacca tggggcgggag cgagcttctt cctgnaccg ggggtggcana nganagccta	300
nctgagggtt cacactataa acgttaacga cnagatnan cacctgttc aagtgcaccc	360
ttccctacgt acnaccagn accnnnaact gcngcctgg gacagcnctg ggancagcta	420
acnnagact cacctgcccc cccatggccg tncgcntccc tggctctgnc aagggaaagct	480
ccctgttggaa attncggggaa naccaaggaa ncccccctctt ccancgttga agggaaaann	540
gatgaaattt tncccttcgg gcnnntcccc tttcccttta cacccccctt nntactcncc	600
tccctctntt ntcctgnenc acttttnacc cnnnnatttc ctttnattga tcggannctn	660
ganattccac tnnccctcnc cnctnatcng naanacnaaa nactntctna cccngggat	720
gggnccctcg ntcatctctt cttttcnctt accnccnntt ctttgccctt cttngatca	780

tccaaacntc gntggccntn cccccccnnn tccttnccc	820
<210> 27	
<211> 818	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(818)	
<223> n = A,T,C or G	
<400> 27	
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tgtttcttc ccgagccca ggcagcggtg attcagccct gcccaacctg attctgatga	120
ctgcggatgc tgcgacggac ccaagggca aatagggtcc cagggtccag ggaggggcgc	180
ctgctgagca ctccgcgcc tcaccctgcc cagccctgc catgagctct gggctgggtc	240
tccgcctcca gggttctgtct ttccangca ngccancaag tggcgctggg ccacactggc	300
ttcttcctgc ccnccttcgt gctctgantc tctgtttcc tgcctgtgc angnccttg	360
gatctcgtt tccctcnctc anngaactct gtttctgann tcttcantta actntgantt	420
tatnacnan tggncgtnc tgtnactt taatggccn gaccggtaa tccctccctc	480
nctcccttc anttcnnna accngcttnc cntcntctcc ccntancccg ccngggaaanc	540
ctccttgc ctnaccangg gcnnnnaccg ccncnnctn ggggggcng gtnnctncnc	600
ctgnnnccc cnctcnctn tnectcgtcc nnccnnncgcn nngcannttc nengtccnn	660
tnncttcn ngtntcgnaa ngntcnctn tnnnnnnncn ngntnnntncn tccctctcnc	720
cnnntgnang tnntnnnnnc nengncccc nnncnnnnn nggnnnnnn tctncncngc	780
ccnnnncccc ngnattaagg cctccnnctc cggccnc	818
<210> 28	
<211> 731	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(731)	
<223> n = A,T,C or G	
<400> 28	
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gattnaaccc cattgtatgg agnnaaaggn ttttagggat ttttcgtct ttatcgtat	180
ntanattcct gtnaatcgga aaatnatntt tccncnggaa aatnttgcct ccatccgnaa	240
attntcccg ggtatgtcat ntnggggn cnccangtt tcccaggctg ctanaatcgt	300
actaaagntt naagtgggan tncaaatgaa aacctnnac agagnatccn taccgactg	360
tnnnnnctc tgcctcnnactg actctgcnnng agcccaatac ccnnngngnat gtcnccnng	420
nnngcgnncn tggaaannnncc tgcngctnn gancatcang gggttcgtca taaaagcnn	480
cgttcncat naaggactt tngcctcata caaccnctng ccctcnccca ttngccgtc	540
nggttcncc acgtnnntng cnccnnntn ganatttnc ccgcctnggg naancctct	600
gnaatgggtt gggncnnttc tttnnacnnn gnggtntact aatcnctnc acgcnnttt	660
tctcnacccc ccccccctt caatcccanc ggcnaatggg gtctccnnn cganggggg	720
nnncannnc c	731
<210> 29	
<211> 822	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(822)
<223> n = A,T,C or G

<400> 29
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atntntacnc tcatannctt cnnnacccac tccctttaa cccntactgt gcctatngcn    180
tnnctantct ntgccgcctn cnancacccn gttggccnac cncnngnatt ctcnatctcc    240
tcncatntn gcctananta ngtnacatacc ctatacctac nccaatgcta nnntaancn    300
tccatnantt annntaacta ccactgacnt ngactttcnc atnanctct aattgaatc    360
tactctgact cccacngcct annnattagc ancntcccc nacnatntct caaccaaatc    420
ntcaacaacc tatctanctg ttcnccaacc ntncctccg atccccnnac aaccccccctc    480
ccaaatacc nccacctgac ncctaaccn caccatcccg gcaagccnan ggnccatttan    540
ccactggaat cacnatngga naaaaaaaaac ccnaactctc tanncnnat ctccctaana    600
aatnctctn naatttactn ncantncat caanccacn taaaacnnaa cccctgtttt    660
tanatccctt cttcgaaaa ccnaccctt annncccaac cttngggcc ccccnctnc    720
ccnaatgaag gncncccaat cnangaaacg ncncntgaaaa ancnaggcna anannntccg    780
canatcctat cccttanttn gggncccctt nccnngggcc cc                                822

<210> 30
<211> 787
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(787)
<223> n = A,T,C or G

<400> 30
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ctagagaaga ctttctctcc tactgtcatt atggagccct gcagactgag ggctccctt    120
gtctgcagga ttgtatgtct gaagtcgtgg agtgtggctt ggagctccctc atctacatna    180
gtctggaaagcc ctggaggggcc tctctcgcca gcctcccccct tctctccacg ctctccangg    240
acaccagggg ctccaggccag cccattattc ccagnangac atgggtttc tccacgcgg     300
cccatggggc ctgnaaggcc agggctctt ttgacaccat ctctcccgct ctgcctggca    360
ggccgtggga tccactantt ctanaacggc cggccaccnccg gtgggagctc cagctttgt    420
tcccnntaat gaaggttaat tgcncgttg gcttaatcat ngtcanaac tnttccctgt    480
gtgaaattgt ttntccctc ncncatccnc ncacatacn aaccggaaan cataaagtgt    540
taaagcctgg gggtnccctn nngaatnaac tnaactcaat taattgcgtt ggctcatggc    600
ccgctttccn ttcnngaaaaa ctgtcncctt ctgcnttntt gaatcgccca ccccccenggg    660
aaaagcgggtt tgcncnttng ggggnccctt ccncctcccc cctcnctaan ccctncgcct    720
cggtcggtnc ngtngcggg gaangggnat nnncctccnc naaggggng agnnngntat    780
ccccaaaa

<210> 31
<211> 799
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G

<400> 31

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aacaaaggac tcctgcagcc ttctctgtct gtccttgc gcagggcacat ggggaggcct	180
cccgccagggt gggggccacc agtccagggg tgggagact acanggggtg ggagtgggtg	240
gtggctggtn cnaatggct gncacanate cctacgattc ttgacacctg gatttaccca	300
ggggaccttc tgttctcca ngnnaacttc rttnatctn aaagaacaca actgtttttt	360
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tatggttccg gcccacctt cccntcnaan aagtaattca ccccccccn ccntctntt	480
cctggggccct taantacca caccggaact canttantta ttcatcttng gntgggcttg	540
ntnatcncn cctgaangcg ccaagttgaa aggccacgccc gtncnnctc cccatagnan	600
nttttnnent canctaatgc ccccccngc aacnatccaa tcccccccn tggggcccc	660
agcccanggc ccccgncctg ggnnnccngn cncgnantcc ccaggttctc ccantcngnc	720
ccnnngcnc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn ngtnncnac	780
ctcgcccccc cennncgng	799

<210> 32
<211> 789
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

<400> 32

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ggcaacaggc tccggcggcg gcggcggcg ccttacctgc ggtaccaaatt ntgcagcctc	180
cgctccgcgt tgatnttctt ctgcagctgc aggtacccntt aaaacagggc ctggccntn	240
ggtgggcacc ctgggattttt aattttccacg ggcacaatgc ggtgcancce ccttaccacc	300
natttaggaat agtggtnntt cccnccncg ttggcnactt ccccnctggaa accacttntc	360
gccccctccgg catctggctt taaaccttgc aaacnctggg gccccttttt tggttntnt	420
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ggncatgtc ttncggggt tgctgcnatn tnccatcacct cccggcnca ncaggncac	540
ccaaaaagtcc ttngggccn caaaaaanct ccggggggnc ccagttcaa caaatcattc	600
ccccctggcc cccaaatctt ccccccgnntt nctgggtttt ggaacccacg cctctnnctt	660
tggnngccaa gntggntccc cttcgggccc cccgggtgggc cccnctctaa ngaaaacncc	720
ntccctnnca ccatacccccc nnngnacgnca tancaangna tccctttttt tanaaacggg	780
ccccccncg	789

<210> 33
<211> 793
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(793)
<223> n = A,T,C or G

<400> 33

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gactaaatgc tgatgaactt cccaaatcaga tgagcatgga tgattggcca gaaatgaana	180
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gcacagatgc ctgtgtgact ccgggtctga cttttggagga ggttggatcat catgatcaca	300
acaangaacg gggctcgatc atcaccantg aggacgacg cgtgagcccc cgcctgcac	360

ctctgctgtt	aaacacccca	gccatccctt	cttc当地aaag	ggatccacta	cttcttagagc	420
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tggcgtaatc	atggtcataan	ctgttccctg	tgtgaaaattt	ttatccgctc	acaattccac	540
acaacatacg	anccggaagc	atnaaatttt	aaagcctgn	ggtnccctaa	tgantgaact	600
nactcacatt	aattggctt	gctactg	cccgccttcc	agtccgaaa	acctgtcctt	660
gccagctgcc	nttaatgaat	cnngccaccc	ccccggggaaa	aggcngttt	cttnttgggg	720
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<210>	34					
<211>	756					
<212>	DNA					
<213>	Homo sapien					
<220>						
<221>	misc_feature					
<222>	(1)...(756)					
<223>	n = A,T,C or G					
<400>	34					
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ccaaccacag	ggaccaaagct	gaccaaacag	cagctaattc	tggccctgt	catactggag	180
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cagctcaa	at	tgattacaan	gagcagctcc	ccgagtcage	ctatatgcac	300
cagctttgg	gcctcaac	ccttcctg	ctgtcccaga	accgggtggc	tgantnccac	360
acgganttgg	ancggctgcc	tgcccaanga	catacanacc	aatgtctaca	tcnaccacca	420
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catccccccgc	cgagagctac	accttcttca	ttgacatct	gctcgacact	atcagggatg	540
aaaatcgcn	ggttgctcca	gaaagctnc	aaaanatcc	tttcnctga	aggccccccgg	600
atncnctagt	ntagaatcg	gcccgcac	gccccgganc	ctccaaac	tcgttnccct	660
ttactgaggg	tnattgccc	cccttggcgt	tatcatggc	acnccngttn	cctgtgttga	720
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<210>	35					
<211>	834					
<212>	DNA					
<213>	Homo sapien					
<220>						
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<222>	(1)...(834)					
<223>	n = A,T,C or G					
<400>	35					
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ggaanc	cg	ttcccttcc	tgaannaact	ttgaccgtng	gaatagccgc	660
acntnctgg	ccgggttcaa	antccctcn	ttgnccnntc	cctcgggcca	ttctggattt	720
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gctnttggcc antcccctgg gggcntntan cnccccctnt ggtcccnntng ggcc	834
<210> 36	
<211> 814	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(814)	
<223> n = A,T,C or G	
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naacgccaac tcaggccatt cctaccaaag gaagaaaaggc tggctctcc acccccgtta	180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat cttaagtctt gtgtttact	240
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccc cagcctggca	300
ctaaaacanc ccagcgctca cttctgttg ganaaatattt ctttgcctt ttggacatca	360
ggcttgatgg tatcaactgcc acnnttccac ccagctggc nccttcccc catntttgtc	420
antganctgg aaggcctgaa ncttagtctc caaaaagtctc ngeccacaag accggccacc	480
aggggangtc nttnncatgt gatctgcca anantacccn tatcatcnnt gaataaaaag	540
gcccctgaac ganatgctc cancancctt taagacccat aatcctngaa ccatgggtcc	600
cttcggct gatccnaaag gaatgttctt gggtcccant ccctcccttg ttntttacgt	660
tgtnttggac ccntgctngn atnacccaan tganatcccc ngaagcaccc tnccctggc	720
atttgantt cntaaattct ctgcctcaen nctgaaagca cnattccctn ggcnccnaan	780
ggngaactca agaaggtctn ngaaaaacca cncn	814
<210> 37	
<211> 760	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(760)	
<223> n = A,T,C or G	
<400> 37	
gcatgtgtcttccaaa gttgttcttgg ttgccataac aaccaccata ggtaaagcgg	60
gcfgcagtgtt cgctgaaggg gttgtgtac cagcgcggga tgctctccctt gcagagtcct	120
gtgtctggca ggtccacgca atgccccttg tcaactggggaa aatggatgcg ctggagctcg	180
tcnaanccac tcgtgttattt ttcacangca gcctcctccg aagcntccgg gcagttgggg	240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt	300
gggctgacag gtgccagaac acactggatn ggccttcca tggaaaggcc tggggaaat	360
cncctnancc caaaactgcct ctcaaaggcc accttgcaca ccccgacagg ctagaaatgc	420
actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aacccaaaanc	480
ttgaaaaatc tgctccgtgg gggtcatnnn taccanggtt gggaaaanaa accccggcngn	540
gancncctt gtttgaatgc naaggnaata atcctctgt ctgttggg tggaaanagca	600
caattgaact gttAACNTTG ggccgngttc cnctnggggtg gtctgaaact aatcacggc	660
actggaaaaa ggtangtgc ttcccttgaat tcccaaantt cccctngntt tgggnnttt	720
ctccctncc ctaaaaatcg ntntcccccc cnctanggc	760
<210> 38	
<211> 724	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(724)
<223> n = A,T,C or G

<400> 38
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cttcnnaaat tgtccaaccc ctctnnccaa atnnccattt ccgggggggg gttccaaacc 120
caaattaatt ttggantttt aattaaatnt tnattnnggg aanaanccaa atgtnaagaa 180
aatttaaccc attatnaact taaatncctn gaaacccntg gnttccaaaaa atttttaacc 240
cttaaatccc tccgaaattt gtaangaaa accaaattcn cctaagctn tttgaaggtt 300
ngatttaaac ccccttnant nttnnacc cnngnctnaa ntattnngt tccgggttt 360
tcctnttaan ctnnggttaac tccccnta gaannncctt aanccaatta aaccgaattt 420
ttttgaatt gaaaattccn ngggattna cccgggtttt tcccnnnttgg gggccatncc 480
cccncnttcg gggtttgggn ntaggttga ttttnnang ncccaaaaaa ncccccaana 540
aaaaaaactcc caagnnttaa ttngaatntc ccccttccca ggcctttgg gaaaggmngg 600
ttntggggg cnngggantt ctncccccnn ttnccncccc ccccccnggt aaanggttat 660
ngnnttggt ttttggggccc cttnanggac ctcccgatn gaaattaaat ccccggnmcg 720
gccg                                724

<210> 39
<211> 751
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(751)
<223> n = A,T,C or G

<400> 39
ttttttttt tttttctttt ctcacattt aaaaaaaaaa tgatTTTTT taatgctgca      60
caacacaata ttatTTcat ttgtttcttt tatttcattt tattttgttt ctgtgtgtgt 120
tttattttt tttactgaaa gtgagaggga acctttgtgg cctttttcc tttttctgtta 180
ggccgcctt a gctttctaa atttggaaaca tctaagcaag ctgaangggaa aagggggttt 240
cgaaaaatca ctcgggggaa ngggaaagggtt gctttgttaa tcatgcctt tgggtgggtga 300
ttaactgctt gtacaattac ntTCacttt taattaattt tgctnaangc tttaattana 360
cttgggggtt ccctccccan accaaccnnn ctgacaaaaaa gtgcengccc tcaaattnatg 420
tccggcnnnt ctttgcacca cacngcngaa ngttcttcatt ntccccnnnc cagtnaaaaa 480
tgaagggtta ccatnnttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn 540
ccctcaancn aattnctnnn ccccggtcnc gentnnngtcc cncccggtt ccgggaantn 600
caccnccngaa annccnnnnn naacnaaaattt ccgaaaatattt tcccnntcnc tcaattcccc 660
cnnagactnt ctcnnnnnan cncaattttt ttttnntcac gaacncgnnc cnnaaaatgn 720
nnnnccnccctc cnctngtccn naatcnccan c                                751

<210> 40
<211> 753
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(753)
<223> n = A,T,C or G

<400> 40
gtggatTTTT ctgttaagatc aggtgttcct ccctcgtagg ttttagaggaa acaccctcat      60
agatgaaaac ccccccggaga cagcagcaact gcaactgcca agcagccggg gtagggagggg 120

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cgccttatgc acagctggc cttttagaca gcagggttc gatgtcaggc tcgtatgtcaa	180
tggctggaa gcggcggtg tacctgcgtt ggggcacacc gtcaggcccc accaggaact	240
tctcaaaagt ccaggcaacn tcgtgcgtac acaccggaga ccaggtgatn agcttgggt	300
cggtcataan cgccgtggc tcgtcgctgg gagctggcag ggcctccgc aggaaggcna	360
ataaaaaggta cgcccccgca ccgttcanct cgcacttctc naanaccatg angttggct	420
cnaaccacc accannccgg acttccgttga nngaattccc aaatcttgc gntcttggc	480
ttctnctgat gccctanctg gttggccngn atgccaanca nccccaanc cccgggtct	540
aaancacccn cctctctt tcatctgggt ntntntcccc ggaccntggt tctctcaag	600
gganccata tctcnaccan tactcacnt nccccccnt gnnaccanc ctcttanngn	660
ttcccncccg nectctggcc cntcaaanan gttncacna cctgggtctg cttttttttt	720
tnccttatct gnaccccn cn tttgtctcan tnt	753
<210> 41	
<211> 341	
<212> DNA	
<213> Homo sapien	
<400> 41	
actatatcca tcacaacaga catgtttcat cccatagact tcttgacata gcttcaaatg	60
agtgaaccca tccttgattt atatacatat atgttctca gatgttggaa gcctttccac	120
ttctttaaac cttgttcattt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt	180
tatagcttgtt ttacgttagta agttttgaa gtctacattt aatccagacca ctttagtttag	240
tgttaaactg tgattttaaa aaaatatcat ttgagaatat tctttcagag gtatttcat	300
ttttactttt tgattaattt tgatggat attaggtag t	341
<210> 42	
<211> 101	
<212> DNA	
<213> Homo sapien	
<400> 42	
acttactgaa tttagttctg tgctottcct tatttagtgt tttatcataa atactttgat	60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a	101
<210> 43	
<211> 305	
<212> DNA	
<213> Homo sapien	
<400> 43	
acatctttgt tacagtctaa gatgtgttct taaatcacca ttcttcctg gtctcaccc	60
tccagggtgg ttcacactg taatttagac tatttggagg tctttacagc aaattaagat	120
tcagatgcct tgctaaatgtt agagttctag agttatgtt cagaaagtct aaaaaaccca	180
cctttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat	240
tggatacaga acgagagttt tcctggataa ctcagagctg agtacctgcc cggggccgc	300
tcgaa	305
<210> 44	
<211> 852	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(852)	
<223> n = A,T,C or G	
<400> 44	

acataaaat cagagaaaag tagtcttga aatatttacg tccaggagtt ctttgttct	60
gattattgg tgtgtgttt ggtttgtgc caaagtatttgcagcttcag tttcatttt	120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct	180
ccagaatttc tctttgttag taatatctca tagctcggtc gagctttca taggtcatgc	240
tgcgttgtt ctctttta ccccatagct gagccactgc ctctgatttc aagaacctga	300
agacgccctc agatcggtct tcccattta ttatcctgg gttcttgtct gggttcaaga	360
ggatgtcgcg gatgaattcc cataagttag tccctctcg gttgtgttt ttgggtgtggc	420
acttggcagg ggggtcttgc tcctttca tatcagggtga ctctgcaaca ggaagggtgac	480
tgggtgtgt catggagatc tgagccggc agaaagtttt gctgtccaac aaatctactg	540
tgctaccata gtttgtgtca tataaatagt tctngtctt ccaggtgttc atgatggaag	600
gctcagtttgc ttcagtcttgc acaatgacat tttgtgttgc ctggAACAGGGTCAAGG	660
actggccgtt ccacttcaga tgctgcaagt tgctgttagag gagntcccccc ggcgtccctg	720
ccgccccgggtt gaactcctgc aaactcatgc tgcaaaagggtt ctcggcgttgc atgtcgaaact	780
cntgaaagg gataacaatttgcatccagct ggttgtgtc caggagggtga tggagccact	840
cccacacactg gt	852

<210> 45

<211> 234

<212> DNA

<213> Homo sapien

<400> 45

acaacagacc ttgctcgct aacgaccta tgctcatcaa gttggacgaa tccgtgtccg	60
agtctgacac catccggagc atcagcatttgc cttcgactgt ccctaccgcg gggaaacttt	120
gcctcggttgc tggctgggggt ctgctggcga acggcagaat gcctaccgtg ctgcgtgcg	180
tgaacgtgtc ggttgtgtctt gaggaggtctt gcaacttgc ctatgacccgc ctgt	234

<210> 46

<211> 590

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(590)

<223> n = A,T,C or G

<400> 46

actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atgggtgtgt	60
attttagatc aatattttgg agattacaga gtttttagaa ttaccaatta cacagttaaa	120
aagaagataa tatattccaa gcanatacaa aatatactaa gaaagatcaa ggcaggaaaa	180
tgantataac taatttgacaa tggaaaatca attttatgtt gaattgcaca ttatccttta	240
aaagcttca aaanaaaanaa ttattgcagt ctanttaattt caaacagtgt taaatggat	300
caggataaaan aactgaaggg canaaagaat taattttcac ttcatgttaac ncacccanat	360
ttacaatggc ttaaatgcan gggaaaaagca gtggaaagttag ggaagtantic aagtttttc	420
tggctcttaa tctgccttac tctttgggtt tgctttgtat cctctggaga cagctgccag	480
ggctcctgtt atatccacaa tccacgcagc aagatgaagg gatggaaaag gacacatgt	540
gccttcctt gaggagactt catctactg gccaacactc agtcacatgt	590

<210> 47

<211> 774

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(774)

<223> n = A,T,C or G

<400> 47
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 tgaacagaat ttccctgnac aacggggctt caaaaataatt ttcttgaaa ggttcaagac 120
 gcttcactgc ttgaaactt aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180
 cattacagac gggactctgg gaggaaaggat aaacagaaaag gggacaaaagg ctaatccaa 240
 aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagtctt ccagggctct 300
 cctcatccct ggaggacac agtgaggaa caactgacca tgcgtccagg ctctgtgtg 360
 ctggctctg gtcttcagcc cccagctctg gaagccccacc ctctgtgtat ctcgtggc 420
 ccacactctt tgaacacaca tccccaggtt atattcctgg acatggctga acctcttatt 480
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccaactcac cctccaaacc 540
 acggcatggg aaggctttct gacttgcctg attactccag catcttggaa caatccctga 600
 ttccccactc ctttagaggca agatagggtg gtttagagta gggctggacc acttggagcc 660
 aggtctgtgg cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct 720
 tcacttctat gggcncattt ttgttctacc tgcaaaatgg gggataataa tagt 774

<210> 48
 <211> 124
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(124)
 <223> n = A,T,C or G

<400> 48
 canaaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120
 tggt 124

<210> 49
 <211> 147
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(147)
 <223> n = A,T,C or G

<400> 49
 gccgatgcta ctatttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt 60
 tgtggctaca ggtgggtct gactgcatna aaaantttt tacgggtat tgcaaaaatt 120
 ttagggcacc catatccaa gcantgt 147

<210> 50
 <211> 107
 <212> DNA
 <213> Homo sapien

<400> 50
 acattaaatt aataaaagga ctgttgggt tctgctaaaa cacatggctt gatatattgc 60
 atgggtttagt gtttagggat gtttaggcata tggggat gagggt 107

<210> 51
 <211> 204
 <212> DNA

<213> Homo sapien

<400> 51

gtccttagaa gtcttagggaa cacacgactc tggggtcacg gggccgacac acttgcacgg	60
cgggaaggaa aggccagagaa gtgacaccgt cagggggaaa tgacagaag gaaaatcaag	120
gccttgcaag gtcagaaagg ggactcaggg ctccaccac agccctgccc cacttggcca	180
cctccctttt gggaccagca atgt	204

<210> 52

<211> 491

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(491)

<223> n = A,T,C or G

<400> 52

acaaaagataa catttatctt ataacaaaaa ttgtatagtt ttaaaggta gtattgtgt	60
gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca	120
ccatcagaca gtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa	180
aaaacttctt gtatcaattt cttttttca aaatgactga cttaatatt tttaaatatt	240
tcanaaacac tccctcaaaa atttcaana tggtagctt canatgncc ctcagtccca	300
atgttgctca gataaataaa tctcgtaga acttaccacc caccacaagc tttctgggc	360
atgcaacagt gtctttctt tncttttct tttttttt ttacaggcac agaaactcat	420
caattttatt tggataaccaa agggtctcca aattatattg aaaaataaaat ccaagttaat	480
atcactcttg t	491

<210> 53

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(484)

<223> n = A,T,C or G

<400> 53

acataatttgcaggcataa ttaccataag atgctattta ttaanaggtt tatgatctga	60
gtattaacag tgcgtgaagt ttggtagttt tatgcagcat tttctttttt ctttgataac	120
actacagaac cctaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgt	180
caatcaaattc tctacataac actatagtaa ttaaaacgtt aaaaaaaaaagt gttgaaatct	240
gcactagtat anaccgctcc tgtcaggata anactgctt ggaacagaaa gggaaaaanc	300
agctttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttgc gcctctccct	360
aatgattggc aggtcnggta aatnccaaa catattccaa ctcaaacactt ctttccncg	420
tancttgant ctgtgtattt caggancagg cgatggaat gggccagccc ncggatgttc	480
cant	484

<210> 54

<211> 151

<212> DNA

<213> Homo sapien

<400> 54

actaaacctc gtgcttgtga actccatata gaaaacggtg ccatccctga acacggctgg	60
ccactggta tactgctgac aaccgcaaca aaaaaacac aaatccttgg cactggctag	120

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tctatgtcct ctcagaatgcc tttttgttg t          151
<210> 55
<211> 91
<212> DNA
<213> Homo sapien

<400> 55
acctggcttg tctccgggtg gttccggcg cccccccacgg tccccagaac ggacactttc      60
gcctccagt ggatactcga gccaaagtgg t          91

<210> 56
<211> 133
<212> DNA
<213> Homo sapien

<400> 56
ggcgatgtg cgttggttat atacaatat gtcattttat gtaaggact ttagtatact      60
tggatttttg gtagtctgtgg gttggggggca cggtccaggg accaataccc catggatacc 120
aaggacaac tgt          133

<210> 57
<211> 147
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

<400> 57
actctggaga acctgagccg ctgctccgccc tctggatga ggtgatgcan gcngtggcgc      60
gactgggagc tgagcccttc cctttgcggcc tgcctcagag gattgttgcc gacntgcan     120
tctcantggg ctggatncat gcagggt          147

<210> 58
<211> 198
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(198)
<223> n = A,T,C or G

<400> 58
acagggatat aggtttaag ttattgtnat tgaaaatac attgaatttt ctgtatactc      60
tgattacata catttaccc ttaaaaaaga tgaaaatctt aattttatg ccacatatta    120
atttaccaat gagttaccc ttggatgaga agtcatgata gcactgaatt ttaacttagtt   180
ttgacttcta agtttggt          198

<210> 59
<211> 330
<212> DNA
<213> Homo sapien

<400> 59

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acaacaaatg gggtgtgagg aagtcttatac agcaaaaactg gtgatggcta ctgaaaagat	60
ccatgaaaa ttatcattaa tgatttaaa tgacaagttt tcaaaaactc actcaatttt	120
cacctgtgct agcttgctaa aatggagttt aactcttagag caaatatagt atcttctgaa	180
tacagtcaat aaatgacaaa gccaggccct acaggtggttt tccagactttt ccagaccagg	240
cagaaggaatt ctatTTTATC acatggatctt ccgtctgtgc tcaaaaatacc taatgtatTTT	300
tttcgtctttt attggacttc tttgaagagt	330
<210> 60	
<211> 175	
<212> DNA	
<213> Homo sapien	
<400> 60	
accgtgggtg ccttctacat tcctgacggc tccttcacca acatctggttt ctacttggc	60
gtcggtggctt ctttccttcatc cagctgggtgc tgctcatcga ctttgcgcac	120
tccttggaaacc agcgggtggctt gggcaaggcc gaggagtgcg attccctgtgc ctgg	175
<210> 61	
<211> 154	
<212> DNA	
<213> Homo sapien	
<400> 61	
acccccacttt tcctcctgtg agcagtctgg acttctcaact gctacatgat gagggtgagt	60
gggttggctt cttcaacagt atcccccctt ttccggatctt gctgagccgg acagcagtgc	120
tggactgcac agccccgggg ctccacattt ctgt	154
<210> 62	
<211> 30	
<212> DNA	
<213> Homo sapien	
<400> 62	
cgctcgagcc ctatagttagtgc tcgtattttaga	30
<210> 63	
<211> 89	
<212> DNA	
<213> Homo sapien	
<400> 63	
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ctgtatgaat aaaaatggttt atgtcaagt	89
<210> 64	
<211> 97	
<212> DNA	
<213> Homo sapien	
<400> 64	
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaaataaa ggttctgcag	60
aatcagtgcattt tccaggattt gtccttggat ctgggg	97
<210> 65	
<211> 377	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(377)
<223> n = A,T,C or G

<400> 65
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gcatggcgtc ctaggccttg acacagcggc tgggggtttgg gctntccaa accgcacacc      120
ccaaccctgg tctaccacca ntctggcta tgggctgtct ctgccactga acatcagggt      180
tcggtcataa natgaaatcc caangggac agaggtcagt agaggaagct caatgagaaa      240
ggtgtctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg      300
tgggggtgaa ctaccccan gaggaatcat gcctggcga tgcaanggtg ccaacaggag      360
ggcgccggagg agcatgt      377

<210> 66
<211> 305
<212> DNA
<213> Homo sapien

<400> 66
acgcctttcc ctcagaattc agggaaagaga ctgtcgctg cttccctccg ttgttgcgtg      60
agaacccgtg tgcccccttc caccatatcc accctcgctc catcttgaa ctcaaacacg      120
aggaactaac tgcacccctgg tcctctcccc agtccccagt tcaccctcca tccttcaccc      180
tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt      240
ttatataattt ttaataaga tgcactttat gtcattttt aataaagtct gaagaattac      300
tgttt      305

<210> 67
<211> 385
<212> DNA
<213> Homo sapien

<400> 67
actacacaca ctccacttgc ctttgagaa cactttgtcc cagcactta ggaatgctga      60
ggtcggacca gcccacatctc atgtgcaaga ttgcccagca gacatcaggctgagatcc      120
ccctttaaa aaaggggact tgctaaaaaa agaagtctag ccacgattgt gtagagcagc      180
tgtgctgtgc tggagattca ctttgagag agttctctc tgagacctga tcttagagg      240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgctt      300
cctctccca ggcggcagcc tggccacacc tgcttacagg gcaactctc tagtccatac      360
catagtttct gtgcttagtgg accgt      385

<210> 68
<211> 73
<212> DNA
<213> Homo sapien

<400> 68
acttaaccag atatatttt accccagatg gggatattct ttgtaaaaaaaaa tgaaaataaa      60
gttttttaa tgg      73

<210> 69
<211> 536
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(536)

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<223> n = A, T, C or G

<400> 69

actagtcccg	tgtggtgaa	ttccattgtg	ttgggggctc	tcaccctcct	ctccctgcagc	60
tccagcttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccggttggc	atctataacg	cagaccta	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	tttttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgtcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtccct	gggtgaaatc	caggtgtcaa	gaaatcttan	ggatctgttgc	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccctta	acagggcccc	tctcagccct	cctaattgacc	tccggcctag	ccatgtgatt	60
tcacttccac	tccataaacgc	tcctcataact	aggcctacta	accaacacac	taaccatata	120
ccaatgtgg	cgcgatgtaa	cacgagaaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	ttagaagttt	tttttttcgc	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	tacccccc当地	ctaggaggc	300
actggccccc	aacaggcata	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgttattact	cgcatacagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctatttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) . . . (533)

<223> n = A, T, C or G

<400> 71

agagctata	gtacagtgt	atctcagctt	tgcaaacaca	ttttctacat	agataagtact	60	
aggtaata	agatatgtaa	agaaaagaaaat	cacaccatta	ataatggtaa	gattggttta	120	
tgtgat	ttttgtgtat	tggcacccctt	atatatgttt	tccaaacttt	cagcagtgtat	180	
attat	ttcca	taactaaaa	agttagttt	aaaaagaaaa	tctccagcaa	gcatctcatt	240
taaataaagg	tttgcata	ttaaaaatac	agcaatatgt	gactttttaa	aaaagctgtc	300	
aaatagggtgt	gaccctacta	ataattatta	gaaatacatt	aaaaaacatc	gagtacctca	360	
agtca	gtttagttt	tatcaaata	aactctttaga	gaaatgtaca	taaaagaatg	420	
cttcgt	taatt	ttggagtgang	aggttccctc	ctcaat	ttttagttaaa	aagtacatgg	480
taaaaaaaaaa	aattcacaac	agtatataa	gctgtaaaat	gaagaatt	tc	533	

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) . . . (511)

<223> n = A, T, C or G

<400> 72

tattacggaa	aaacacacca	cataattcaa	ctancaaaaga	anactgcttc	agggcgtgta	60
aatgaaaagg	cttccaggca	gttatctgat	taaagaacac	taaaagaggg	acaaggctaa	120
aagccgcagg	atgtctacac	tatancaggc	gctatttggg	ttggctggag	gagctgtgga	180
aaacatggan	agattggtgc	tgganatcgc	cgtggctatt	cctcattgtt	attacanagt	240
gaggttctct	gtgtgcccac	tggttgaaa	accgttctnc	aataatgata	gaatagtaca	300
cacatgagaa	ctgaaatggc	ccaaacccag	aaagaaagcc	caactagatc	ctcagaanac	360
gcttcttaggg	acaataaccg	atgaagaaaa	gatggcctcc	ttgtcccccc	gtctgttatg	420
atttctctcc	attgcagcna	naaacccgtt	cttctaagca	aacncagggt	atgatggcna	480
aaatacaccc	cctcttgaag	naccngagg	a			511

<210> 73
<211> 499
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(499)
<223> n = A,T,C or G

<400> 73

cagtgccagc	actggtgcca	gtaccagtac	caataacagt	gccagtgccca	gtgccagcac	60
cagtggtggc	ttcagtgtcg	gtgcacgcct	gaccgcact	ctcacatgg	ggctcttcgc	120
tggccttgg	ggagctgggt	ccagcaccag	tggcagctct	ggtgcctgtg	gtttcttcata	180
caagtggat	tttagatatt	gttaatccctg	ccagtttttc	tcttcagatcc	agggtgcata	240
ctcagaaacc	tactcaacac	agcaactctag	gcagccacta	tcaatcaatt	gaagttgaca	300
ctctgcatta	aatcttattt	ccatttctga	aaaaaaaaaa	aaaaaaaaagg	cggccgctcg	360
antctagagg	gcccgtttaa	acccgctgat	cagectcgac	tgtgccttct	anttgcacgc	420
catctgttgt	ttggccctcc	cccgntgcct	tccttgaccc	tggaaagtgc	cactcccact	480
gtcccttcct	aantaaaat					499

<210> 74
<211> 537
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(537)
<223> n = A,T,C or G

<400> 74

tttcatagga	gaacacactg	aggagatact	tgaagaattt	ggattcagcc	gcgaagagat	60
ttatcagctt	aactcagata	aaatcattga	aagtaataag	gtaaaagcta	gtctctaact	120
tccaggccca	cggctcaagt	gaatttgaat	actgcattta	cagtgttagag	taacacataaa	180
cattgtatgc	atggaaacat	ggaggaacag	tattacagtg	tcctaccact	ctaatcaaga	240
aaagaattac	agactctgat	tctacagtga	tgattgaatt	ctaaaaatgg	taatcattag	300
ggctttgtat	ttataanact	ttgggtactt	atactaaatt	atggtagtta	tactgccttc	360
cagtttgcctt	gatatatattt	ttgatattaa	gattcttgac	ttatattttg	aatgggttct	420
actaaaaaan	gaatgtatata	ttcttgaaga	catcgatata	catttattta	cactcttgat	480
tctacaatgt	agaaaaatgaa	ggaaatgccc	caaattgtat	ggtgataaaaa	gtcccggt	537

<210> 75
<211> 467
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(467)
<223> n = A,T,C or G

<400> 75
caanacaat tgccaaaatg atgcaaatga tacactactg ctgcagctca caaacaccc
tgcattttac acgtacccctc tcctgctcct caagtagtgt ggtctatttt gccatcatca
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg
tggcacaagg agggcatctt tcctcatacg gttattgtcc cttagaagcgt cttctgagga
tctatgtggg ctttcttctt gggtttgggc catttcantt ctatgtgtg tactattcta
tcattattgt ataacggttt tcaaaccnngt gggcacncag agaacacctac tctgtataaa
caatgaggaa tagccacggt gatctccagc accaaatctc tccatgtnt tccagagctc
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 60
120
180
240
300
360
420
467

<210> 76
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

<400> 76
aagctgacag cattcgggcc gagatgtctc gtcgtggc ctttagctgtg ctcgcgtac
tctcttttc tggcctggag gctatccagc gtactccaaa gattcaggt tactcacgtc
atccagcaga gaatggaaag tcaaattttcc tgaatttgcta tgtgtctggg tttcatccat
ccgacatgtg agttgactt ctgagaatg gagagagaat taaaaaaagt gggcattcag
acttgtctt cagcaaggac tggctttctt atctcttgcg ctacactgaa ttccccccca
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac ttgtcagc cccaaagatng
tttagtggga tccanacatg taaggcagcan catggggaggt 60
120
180
240
300
360
400

<210> 77
<211> 248
<212> DNA
<213> Homo sapien

<400> 77
ctggagtggc ttgggttttc aagccccctgc aggaagcaga atgcacccccc tgaggcacct
ccagctggcc cggcggggggta tgcgaggctc ggagcacccct tgcccggtcg tgattgtgc
caggcactgt tcatctcagc ttttctgtcc cttagtccccc ggcacgcgt tctgtctgaaa
gttcatatct ggagcctgat gtcttaacga ataaagggtcc catgctccac ccgaaaaaaaaa
aaaaaaaaa 60
120
180
240
300
360
400

<210> 78
<211> 201
<212> DNA
<213> Homo sapien

<400> 78
actagtccag tgggtggaa ttccattgtg ttggggccaa cacaatggct acctttaaca
tcacccagac cccgccccctgc ccgtggccca cgctgctgtc aacgacagta tgatgttac
tctgtactc gggaaactatt tttatgtaat taatgtatgc tttttgttt ataaatgcct
gataaaaaaa aaaaaaaaaa a 60
120
180
201

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<210> 79
<211> 552
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(552)
<223> n = A,T,C or G

<400> 79
tcctttgtt aggttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg      60
tttaggcagt gctagtaatt tcctcgtaat gattctgtt ttactttcct attctttatt     120
cctcttctt ctgaagatta atgaaggtaa aaattgagggt ggataaatac aaaaaggtag     180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt    240
atgcaagttt gtaattactc agggtaact aaattacttt aatatgctgt tgaacctact    300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agttgggaa gccaaattga     360
taatattcta tggtctaaaa gttgggctat acataaaanta tnaagaaaata tgaatttta    420
ttcccaggaa tatgggggttc atttatgaat antaccggg anagaagttt tgantnaaac    480
cngttttgtt taatacgtt atatgtcctn aatnaacaag gcntgactta tttccaaaaaa   540
aaaaaaaaaa aa                                         552

<210> 80
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

<400> 80
acagggattt gagatgctaa ggccccagag atcgtttgc ccaaccctct tattttcaga      60
ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct    120
cacacagact cccgagtagc ttggactaca ggcacacagt cactgaagca ggcctgttt     180
gcaattcagc ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta    240
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt acttcatac    300
tcttctaagt cctcttccag cctcactttg agtcctcctt gggggtgtat aggaantnc    360
tcttggcttt ctcataaaaaa tctctatcca tctcatgttt aatttggtagc gcntaaaaat   420
gctgaaaaaaaaa ttAAAATGTT ctggtttncn ttAAAAAAaaa aaaaaaaaaa aaaaaa    476

<210> 81
<211> 232
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

<400> 81
tttttttttg tatgcncnctn ctgtggngtt attgttgctg ccaccctgga ggagcccagt    60
ttcttctgtt tctttctttt ctggggatc ttccctggctc tgccccctcca ttcccagcct    120
ctcatccccca tcttgcactt ttgtctaggggt tggaggcgct ttccctggtag cccctcagag   180
actcagtcag cgggaataag tccttaggggt ggggggtgtg gcaagccggc ct             232

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<210> 82
<211> 383
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

<400> 82
aggcgggagc agaagctaaa gccaaagccc aagaagagtgcagtgccactgggtgcc      60
agtaccagta ccaataacat gccagtgcac gtgcgcagcac cagtgggtggcttcaagtgcgtg 120
gtgcgcgcct gaccgcact ctcacatttgcgtcttcgc tggccttgggtggagctgggtg 180
ccagcaccag tggcagctct ggtgcctgtgtttcttcata caagttagat ttttagatatt 240
gttaatctcg ccagtctttc tcttcagacc agggtgcatc ctcagaaacc tactcaacac 300
agcactctng gcagccacta tcaatcaatttgaagttgaca ctctgcatttaaatctatttgc 360
ccatttcaaa aaaaaaaaaaaa aaa                                         383

<210> 83
<211> 494
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(494)
<223> n = A,T,C or G

<400> 83
accgaatttgg gaccgctggc ttataagcgtcatgtccctc cagtttacc tcaacgagca      60
gggagatcga gtctataacgc tgaagaaatt tgacccgatggacaaacaga cctgctcagc 120
ccatcctgtct cggttctccc cagatgacaa atactctcgacccgaatca ccatcaagaa 180
acgcttcaag gtgctcatgacccagcaacc ggcgcctgtctcttgagggt ccttaaactg 240
atgttttc tgccacctgttacccctcgagactccgttacccaaactcttcgactgtg 300
agccctgtatgatgttttgcctccatactcttggcncntcagtctctcgatggattgtt 360
tatgttgtgttgggcaatcatgttggcatcaccatnnaa gggaaacacatttttttttttttttt 420
tttcnccatattttaaatttacnaccagaata ntccagaataaatgaatttga aaaaacttta 480
aaaaaaaaaaa aaaa                                         494

<210> 84
<211> 380
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

<400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacggacag tgacttcccc 60
agtatcctgc gccgcgtcttctaccgtccc tacctgcaga tcttcggca gattccccag 120
gaggacatgg acgtggccct catggagcac agcaactgtctgtggagcc cggcttctgg 180
gcacaccctc ctggggccca ggcggcacc tgcgtctccc agtatgccaacttgcgtgg 240
gtgctgtcc tcgtcatctt cctgctcgatggcaacatcc tgctggcac ttgttcatttgc 300
ccatgttcag ttacacatttgcggaaactac agggcaacag cnatcttac tggaaaggcc 360
agegttnccg cctcatccgg                                         380

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<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

<400> 85
gagtttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcg ttcataccgc      60
tnccatcgta atactgtagg tttgccacca cctcctgcat cttggggcg ctaatatcca      120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcg      180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg acttttattga      240
gtcgattctg catgtccagc aggaggtgt accagctctc tgacagttag gtcaccagcc      300
ctatcatgcc nttaacgtg ccgaagaaca ccgagccttg tgggggggt gnagtctcac      360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa      420
aaagaacacc tccttggaaat gctngccgct cctcgccnt tgggggnngc gcntncctt      480
t                                         481

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 86
aacatcttcc tgtataatgc tgtgtataat cgatccgatn ttgtctgctg agaattcatt      60
acttggaaaa gcaacttnaa gcctggacac tggattaaa attcacaata tgcacactt      120
taaacagtgt gtcaatctgc tcccttactt tgcacatcacc agtctggaa taagggtatg      180
ccctattcac acctgttaaa agggcgctaa gcattttga ttcaacatct tttttttga      240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gtagccaat tcacttttt      300
catgggacag agccatttgaa tttaaaaagc aaattgcata atattgagct ttgggagctg      360
atatntgagc ggaagantag ctttctact tcaccagaca caactccctt catattggaa      420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg      472

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

<400> 87
agaaaaccagt atctctnaaa acaacccttc ataccttgg gacctaattt tgtgtcgctg      60
tgtgtgtcg cgcatttat atagacaggc acatctttt tacttttta aaagctttagt      120
cctcttggt atcttatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcac tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg      300

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ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aatncataa	360
acagaaaattg ggtngtataat tgaaanannng catcattnaa acgtttttt ttt	413
<210> 88	
<211> 448	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(448)	
<223> n = A,T,C or G	
<400> 88	
cgcagcgggt cctctctatc tagctccagc ctctcgctg ccccactccc cgctgtccccgc	60
gtcctagccn accatggccg ggccctgcg cggcccgctg ctccctgtgg ccatactggc	120
cgtggccctg gccgtgagcc cgcgcggcgg ctccagtcgg ggcaggccgc cgccgtgg	180
gggaggccca tggaccggcgt gtggagaag aagggtgtgcg gctgtcactg gactttgcgg	240
tcggcnanta caacaaacccc gcaacnactt ttaccnagcn cgctgtcag gttgtccgc	300
cccaanacaa ttgttactng gggtaantaa ttcttggaaag ttgaacctgg gccaaacnnng	360
tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagccctt tttaaaaagg	420
gaancantcc tgntcttttcaaaatttt	448
<210> 89	
<211> 463	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(463)	
<223> n = A,T,C or G	
<400> 89	
gaattttgtg cactggccac tgtgtatggaa ccattgggcc aggatgttt gagtttatca	60
gtatgtattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaatttagc	120
agagggtctag gtctgcataat cagcagacag tttgtccgtg tattttgttag ccttgaagtt	180
ctcagtgaca agtttnntct gatgcgaagt tctnattcca gtgttttagt ccttgcatac	240
tttnatgttn agacttgcct ctnnaaattt gctttgtnt tctgcaggta ctatctgtgg	300
ttaacaaaa tagaannact tctctgtctn gaanatttga atatcttaca tctnaaaatn	360
aattctctcc ccatannaacc acccangccc ttggganaat ttgaaaaang gntccttcnn	420
aattcnnana anttcagnnt tcataacaaca naacngganc ccc	463
<210> 90	
<211> 400	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(400)	
<223> n = A,T,C or G	
<400> 90	
agggattgaa ggtctntnt actgtcgac tggtcancca ccaactctac aagttgtgt	60
cttcactca ctgtctgtaa gcntnttaac ccagactgtatcttccataaa tagaacaat	120
tcttcaccag tcacatcttc taggacctt ttggattcag ttagtataag ctcttccact	180
tcctttgtta agacttcatc tggtaaagtc ttaagtttg tagaaaggaa tttaattgct	240

cgttctctaa caatgtcctc tccttgaagt atttggctga acaaccacc tnaagtcctc ttgtcatcc atttaata tactaatag ggcattggtn cactaggta aattctgcaa gagtcatctg tctgaaaag ttgcgttagt atatctgcca	300 360 400
<210> 91	
<211> 480	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(480)	
<223> n = A,T,C or G	
<400> 91	
gagctcgat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact ggcttacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtccagac atgccttctt gactaccgtg tgccagtgtc ggtgattctc acacacctcc nnccgcttctt tggtggaaaa ctggcacttg nctggaaacta gcaagacatc acttacaaat tcacccacgaa gacacttggaa aggtgtaaaca aagcgactct tgcatgtt tttgtccctc cggcaccagt tgtcaataact aaccccgctgg tttgcctcca tcacatttgc gatctgtage tctggataca tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt ngatcagggtt cccatattcccc agtccgaatg ttcacatggc atatnttact tcccacaaaaa	60 120 180 240 300 360 420 480
<210> 92	
<211> 477	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(477)	
<223> n = A,T,C or G	
<400> 92	
atacagccca natccccacca cgaagatgcg cttgttgact gagaacctga tgcggtaact ggtcccgctg tagccccagc gactctccac ctgctggaaag cggttgcgtc tgcaactcctt cccaacgcagg cagcagcggg gccggtaat gaactccact cgtggcttgg gggtgacgggt taantgcagg aagaggctga ccacccgcg gtccaccagg atgcccgaact gtgcgggacc tgcagcggaaa ctccctcgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccta gaacacctccg cctgttctct ggcgtcacct gcagctgtc cgcctnacac tcggcctcgg accagcggac aaacggcgtt gaacagccgc acctcacggta tgcccantgt gtcgcgtcc aggaacggcn ccagcgtgtc caggtaatg tcggtaanc ctccgggggtt aatggcg	60 120 180 240 300 360 420 477
<210> 93	
<211> 377	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(377)	
<223> n = A,T,C or G	
<400> 93	
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tgatttact tggaaatttc ctctgtata tagctttcc caatgcta at ttccaaacaa	240
caacaacaaa ataacatgtt tgctgttna gttgtataaa agtangtgat tctgtatnta	300
aagaaaatat tactgttaca tatactgctt gcaanttctg tatttattgg tnctctggaa	360
ataaaatatat tattaaa	377
<210> 94	
<211> 495	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(495)	
<223> n = A,T,C or G	
<400> 94	
cccttgagg ggttagggtc cagttccag tggaaagaaac aggccaggag aantgcgtgc	60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgaccct	120
ccaaggaaag accacacctt ggggacatgg gctggagggc aggacctaga ggcaccaagg	180
gaaggccccca ttccggggct gttcccgag gaggaaggga aggggctctg tttttttttt	240
acgaggaana ggcctgtant cctggatca nacacccctt cacgtgtatc cccacacaaa	300
tgcaagctca ccaaggccc ctctcagtcc cttccctaca ccctgaacgg ncactggccc	360
acacccaccc agancancca cccgccatgg ggaatgtntc caaggaatcg cngggcaacg	420
tggactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana	480
aaaaaaaaaaaaaaa aaaaaa	495
<210> 95	
<211> 472	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(472)	
<223> n = A,T,C or G	
<400> 95	
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc	60
cctctggaaag ctttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt	120
tagctgtttt gagttgattt gcaccactgc accacaactc aatatgaaaa ctattnact	180
tatttattat ctttgtaaaa gtatacaatg aaaattttgt tcataactgtt tttatcaagt	240
atgtgaaaaa gcaatagata tatattttt tattatgttn aattatgatt gccatttata	300
atcgcaaaaaa tttttttttt cacagtaata tatgcctttt gtaacttcac	360
ttttttttttt tattgtaaat gaattacaaa attcttaatt taagaaaaatg gtangttata	420
ttttttttttt can taatttcttt ctttgcattt gttttttt aaaaatgc at	472
<210> 96	
<211> 476	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(476)	
<223> n = A,T,C or G	
<400> 96	
ctgaaggcatt tcttcaaact tntctacttt tgtcattgtt acctgttagta agttgacaat	60

gtgggtgaaat ttcaaaaatta tatgttaactt ctactagttt tactttctcc cccaagtctt 120
 ttttaactca tgatTTTAC acacacaatc cagaacttat tatatagcct ctaagtcttt 180
 attcttcaca gtagatgatg aaagagtctt ccagtgttcc gngcanaatg ttctagntat 240
 agctggatac atacngtggg agttctataa actcatactt cagtggact naaccaaaaat 300
 tgggttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct 360
 gcaggtaactc ctccagaaaa acngacaggg caggcttgcg tgaaaaagtn acatctgcgt 420
 tacaaggctt atcttcctca nangtctgtn aaggaacaat ttaatcttct agcttt 476

<210> 97
 <211> 479
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(479)
 <223> n = A,T,C or G

<400> 97

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 aaataatgc gcaaacttaa tggctttagt caaaatggaa cgctaatgaa acacagctta 120
 caatcgcaaa tcaaaaactca caagtgtca tctgtttagt atttagtgtta ataagactta 180
 gattgtgttc cttcgatata gattgtttct canatcttgg gcaatnttcc ttagtcaaata 240
 caggctacta gaattctgtt attggatata tgagagcatg aaatttttaa naatacactt 300
 gtgattatna aattaaatcac aaatttcaact tatacctgct atcagcagct agaaaaaacat 360
 ntntttta natcaaagta ttttgtttt ggaantgtn aaatgaaatc tgaatgtggg 420
 ttcnatctta tttttcccn gachactant tnctttttt gggncatttc tgancatc 479

<210> 98
 <211> 461
 <212> DNA
 <213> Homo sapien

<400> 98

agtgacttgt cctccaacaa aacccttga tcaagtttg ggcactgaca atcagaccta 60
 tgctagttcc tgcatactat tcgctactaa atgcagactg gaggggacca aaaaggggca 120
 tcaactccag ctggattatt ttggagcctg caaatcttatt cctacttgc cgactttga 180
 agtgatttcag ttccctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta 240
 tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaataaaa gtcaaaaaat 300
 ttacctggag aaaagaggtt ttggctgggg accatccccat tgaaccttct cttaggact 360
 ttaagaaaaa ctaccacatg ttgtgtatcc tggtgcggc cgtttatgaa ctgaccaccc 420
 ttggaaataa tcttgacgct cctgaacttg ctccctctgcg a 461

<210> 99
 <211> 171
 <212> DNA
 <213> Homo sapien

<400> 99

gtggccgcgc gcaggtgttt cctcgataccg cagggcccccc tcccttcccc aggctccct 60
 cggccctct cggggccccga ggaggagcgg ctggcgggtg gggggagtgt gaccacccct 120
 cggtgagaaa agccttctct agcgatctga gaggcgtgcc ttgggggtac c 171

<210> 100
 <211> 269
 <212> DNA
 <213> Homo sapien

<400> 104

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cactctctag atagggcatg aagaaaaactc atcttcagg cttaaaata acaatcaaat	120
ctcttatgtc atatcatatt ttaagttaaa ctaatgagtc actggcttat cttctcctga	180
aggaaatctg ttcatcttc tcattcatat agttatataca agtactacct tgcatattga	240
gaggtttttc ttctcttattt acacatataat ttccatgtga atttgatca aacctttattt	300
ttcatgcaaa ctagaaaata atggttcttt tgcataagag aagagaacaa tatagcatta	360
caaaaactgct caaattgttt gttaagttat ccattataat tagttggcag gagctaatac	420
aaatcacatt tacgacagca ataataaaac tgaagtagcca gttaaatatc caaaataattt	480
aaaggaacat ttttagcctg ggtataatta gctaattcac tttacaagca tttatttagaa	540
tgaattcaca tgtttattt cctagcccaa cacaatgg	578

<210> 105
<211> 538
<212> DNA
<213> Homo sapien

<400> 105

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gaaaagtgcc ttacatttaa taaaagttt tttctcaaag tgatcagagg aatttagat	120
gtcttgaaca ccaatattaa ttggggaaa atacacccaa atacattaag taaatttattt	180
aagatcatag agcttgttaag tgaaaagata aaatttgacc tcagaaactc tgacattaa	240
aaatccacta ttagcaaaa aattactatg gacttcttgc tttatattt tgatgaatat	300
ggggtgtcac tggtaaacca acacattctg aaggatacat tacttagtga tagattctta	360
tgtactttgc taatacgtgg atatgagttt acaagtttct ctttctcaa tcttttaagg	420
ggcgagaaaat gaggaagaaa agaaaaggat tacgcatact gttcttcta tggaaaggatt	480
agatatgttt ctttgccaa tattaaaaaa ataataatgt ttactactag tgaaaccc	538

<210> 106
<211> 473
<212> DNA
<213> Homo sapien

<400> 106

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atttatttagc tctgcaactt acatatttaa attaaagaaa cgtttagac aactgtacaa	120
tttataaaatg taaggtgcca ttatttagta atatattctt ccaagagtgg atgtgtccct	180
tctcccacca actaatgaac agcaacattt gtttaattttt atttagtagat atacactgct	240
gcaaaacgcta attctcttct ccattccccat gtgatattgt gtatatgtgt gagttggtag	300
aatgcacatcac aatctacaat caacagcaag atgaagctag gctggctt cggtaaaaat	360
agactgtgtc tgtctgaatc aaatgatctg acctatcctc ggtggcaaga actcttcgaa	420
ccgcttcctc aaaggcgctg ccacatttg ggctttgc acttggttca aaa	473

<210> 107
<211> 1621
<212> DNA
<213> Homo sapien

<400> 107

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ctgtgtatg gtcctggctg acttcggggc gcgtgtggta cgcgtggacc ggccggctc	120
ccgcgtacgac gtgagccgt tggccgggg caagcgctcg ctagtgcgtt acctgaagca	180
gccgcggggca gcccgggtgc tgcggcgtct gtgcagcgcc tggatgtgc tgctggagcc	240
ttccgcggcgc ggtgtcatgg agaaaactcca gctggggccca gagattctgc agcggggaaaa	300
tccaaaggctt atttatgcca ggctgagtgg atttggccag tcaggaagct tctggccgtt	360
agctggccac gatatcaact atttggctt gtcaggtgtt ctctcaaaaa ttggcagaag	420
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gtgtgcactg ggcattataa tggctttt tgaccgcaca cgcaactgaca agggtcaggt	540

cattgatgca aatatggtgg aaggaacagc atatttaagt tctttctgt gaaaaactca 600
 gaaatcgagt ctgtggaaag cacctcgagg acagaacatg ttggatggtg gagcacctt 660
 ctatacgact tacaggacag cagatgggg attcatggct ttggagcaa tagaacccca 720
 gttctacgag ctgctgatca aaggacttgg actaaagtct gatgaacttc ccaatcagat 780
 gagcatggat gattggccag aaatgaagaa gaagtttgc gatgtatgg caaagaagac 840
 gaaggcagag tgggtgtcaaa tctttgacgg cacagatgcc tgggtgactc cggttctgac 900
 ttttggggag gtgttgtcatc atgatcacaa caaggaacgg ggctcggtta tcaccagtga 960
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 cagccgcgaa gagatttatac agcttaactc agataaaaatc attgaaagta ataaggtaaa 1140
 agctagtctc taacctccag gcccacggct caagtgaatt tgaatactgc atttacagtg 1200
 tagagtaaca cataacattg tatgcatgga aacatggagg aacagtatta cagtgcccta 1260
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 aatggttatac attagggctt ttgattata aactttggg tacttatact aaattatgg 1380
 agttattctg cttccagg tgcgttat atttggat attaagattc ttgacttata 1440
 ttttgaatgg gttctagtga aaaagaatg atatattctt gaagacatcg atatacattt 1500
 atttacactc ttgattctac aatgttagaaa atgaggaaat gccacaaatt gtatggat 1560
 aaaagtacg tgaaacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
 a

<210> 108

<211> 382

<212> PRT

<213> Homo sapien

<400> 108

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Gly	Pro	Phe	Cys	Ala	Met	Val	Leu	Ala	Asp	Phe	Gly	Ala	Arg	Val	Val
					20				25						30
Arg	Val	Asp	Arg	Pro	Gly	Ser	Arg	Tyr	Asp	Val	Ser	Arg	Leu	Gly	Arg
					35			40							45
Gly	Lys	Arg	Ser	Leu	Val	Leu	Asp	Leu	Lys	Gln	Pro	Arg	Gly	Ala	Ala
					50			55							60
Val	Leu	Arg	Arg	Leu	Cys	Lys	Arg	Ser	Asp	Val	Leu	Leu	Glu	Pro	Phe
					65			70							80
Arg	Arg	Gly	Val	Met	Glu	Lys	Leu	Gln	Leu	Gly	Pro	Glu	Ile	Leu	Gln
					85			90							95
Arg	Glu	Asn	Pro	Arg	Leu	Ile	Tyr	Ala	Arg	Leu	Ser	Gly	Phe	Gly	Gln
					100			105							110
Ser	Gly	Ser	Phe	Cys	Arg	Leu	Ala	Gly	His	Asp	Ile	Asn	Tyr	Leu	Ala
					115			120							125
Leu	Ser	Gly	Val	Leu	Ser	Lys	Ile	Gly	Arg	Ser	Gly	Glu	Asn	Pro	Tyr
					130			135							140
Ala	Pro	Leu	Asn	Leu	Leu	Ala	Asp	Phe	Ala	Gly	Gly	Gly	Leu	Met	Cys
					145			150							160
Ala	Leu	Gly	Ile	Ile	Met	Ala	Leu	Phe	Asp	Arg	Thr	Arg	Thr	Asp	Lys
					165			170							175
Gly	Gln	Val	Ile	Asp	Ala	Asn	Met	Val	Glu	Gly	Thr	Ala	Tyr	Leu	Ser
					180			185							190
Ser	Phe	Leu	Trp	Lys	Thr	Gln	Lys	Ser	Ser	Leu	Trp	Glu	Ala	Pro	Arg
					195			200							205
Gly	Gln	Asn	Met	Leu	Asp	Gly	Gly	Ala	Pro	Phe	Tyr	Thr	Thr	Tyr	Arg
					210			215							220
Thr	Ala	Asp	Gly	Glu	Phe	Met	Ala	Val	Gly	Ala	Ile	Glu	Pro	Gln	Phe
					225			230							240
Tyr	Glu	Leu	Leu	Ile	Lys	Gly	Leu	Gly	Leu	Lys	Ser	Asp	Glu	Leu	Pro
					245			250							255

Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala
 260 265 270
 Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
 275 280 285
 Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
 290 295 300
 His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu
 305 310 315 320
 Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala
 325 330 335
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu
 340 345 350
 Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn
 355 360 365
 Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu
 370 375 380

<210> 109
 <211> 1524
 <212> DNA
 <213> Homo sapien

<400> 109

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cagtgcacc	tagtggctc	cacctgttc	ctcctggggcg	tggctgccc	gctgaccccg	180
gttttgcacc	acctggggccg	cactgttc	tgcatacgact	tcatggttt	cacgggtgcgg	240
ctgcgttaca	tcttcacgt	caacaacag	ctggggccca	agatcgat	cgtgagcaag	300
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gtcttctacc	gtccctactt	gcagatctt	ggcagattt	cccaggagga	catggacgtg	480
gccctcatgg	agcacagcaa	ctgctgtcg	gagccggct	tctgggcaca	ccctctgggg	540
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atcttcctgc	tctgtggccaa	catccgtct	gtcaacttgc	tcattggccat	ttcagttac	660
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atccggaaat	tccactctcg	gccccgcgt	gccccggccct	ttatcgat	ctcccaat	780
cgccctctgc	tcaggcaatt	gtgcaggcg	ccccggagcc	cccagccgtc	ctccccggcc	840
ctcgagcatt	tccgggttta	ccttctaa	gaagccgagc	ggaagctgt	aacgtggaa	900
tcgggtgcata	aggagaactt	tctgtggca	cgcgttaggg	acaagcgga	gagcgactcc	960
gagcgctctg	agcgcacgtc	ccagaagg	gacttggcac	tgaaaacat	gggacacatc	1020
cgcgactacg	aacagcgcc	gaaaatgtct	gagcgggagg	tccagcgat	tagcccggtc	1080
ctgggggtgg	tggcccgaggc	cctgagccgc	tctgccttgc	tgccccccagg	tggccgcga	1140
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ccacagggg	ttttgtctt	agagtaaggc	tcatctggc	ctcgcccccc	gcacctgg	1260
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cagagaaaaa	aaaaaaaaaa	aaaaaa				1524

<210> 110
 <211> 3410
 <212> DNA
 <213> Homo sapien

<400> 110

gggaaccacgc	ctgcacgcgc	tggctccggg	tgacagccgc	gcgcctcgcc	caggatctga	60
gtgatgagac	gtgtccccac	tgaggtgccc	cacagcagca	ggtgttgc	atgggctgag	120

<210> 111
<211> 1289

<212> DNA
 <213> Homo sapien

<400> 111

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gtggagcctc	agcagtcccc	tcttcagaa	ctcactgcct	agagccctga	acaggagcca	120
ccatgcagtg	ttcagcttc	attaaagacca	tgtatgatcct	cttcaatttg	ctcatcttcc	180
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tgaagatctt	cgggccactg	tcgtccagtg	ccatgcagtt	tgtcaacgtg	ggctacttcc	300
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gtagccaggt	ctgtgcccc	ttccccccagt	ctattaaacc	cttgatatgc	ccccttagcc	1140
tagggtagt	cccagtgc	tactggggg	tgagagaaaag	gcattttata	gcctgggcat	1200
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tgttacaatg	ttaaaaaaaaaa	aaaaaaaaaa				1289

<210> 112
 <211> 315
 <212> PRT
 <213> Homo sapien

<400> 112

Met	Val	Phe	Thr	Val	Arg	Leu	Leu	His	Ile	Phe	Thr	Val	Asn	Lys	Gln	
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Leu	Gly	Pro	Lys	Ile	Val	Ile	Val	Ser	Lys	Met	Met	Lys	Asp	Val	Phe	
						20				25				30		
Phe	Phe	Leu	Phe	Phe	Leu	Gly	Val	Trp	Leu	Val	Ala	Tyr	Gly	Val	Ala	
						35				40				45		
Thr	Glu	Gly	Leu	Leu	Arg	Pro	Arg	Asp	Ser	Asp	Phe	Pro	Ser	Ile	Leu	
						50				55				60		
Arg	Arg	Val	Phe	Tyr	Arg	Pro	Tyr	Leu	Gln	Ile	Phe	Gly	Gln	Ile	Pro	
65						70				75				80		
Gln	Glu	Asp	Met	Asp	Val	Ala	Leu	Met	Glu	His	Ser	Asn	Cys	Ser	Ser	
						85				90				95		
Glu	Pro	Gly	Phe	Trp	Ala	His	Pro	Pro	Gly	Ala	Gln	Ala	Gly	Thr	Cys	
						100				105				110		
Val	Ser	Gln	Tyr	Ala	Asn	Trp	Leu	Val	Val	Leu	Leu	Leu	Val	Ile	Phe	
						115				120				125		
Leu	Leu	Val	Ala	Asn	Ile	Leu	Leu	Val	Asn	Leu	Leu	Ile	Ala	Met	Phe	
						130				135				140		
Ser	Tyr	Thr	Phe	Gly	Lys	Val	Gln	Gly	Asn	Ser	Asp	Leu	Tyr	Trp	Lys	
145						150				155				160		
Ala	Gln	Arg	Tyr	Arg	Leu	Ile	Arg	Glu	Phe	His	Ser	Arg	Pro	Ala	Leu	
						165				170				175		
Ala	Pro	Pro	Phe	Ile	Val	Ile	Ser	His	Leu	Arg	Leu	Leu	Arg	Gln		
						180				185				190		
Leu	Cys	Arg	Arg	Pro	Arg	Ser	Pro	Gln	Pro	Ser	Ser	Pro	Ala	Leu	Glu	

195	200	205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys	Leu Leu Thr	
210	215	220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp		
225	230	235
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val		
245	250	255
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg		
260	265	270
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly		
275	280	285
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly		
290	295	300
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp		
305	310	315

<210> 113
 <211> 553
 <212> PRT
 <213> Homo sapien

<400> 113		
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala		
1	5	10
Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu		
20	25	30
Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val		
35	40	45
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly		
50	55	60
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly		
65	70	75
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile		
85	90	95
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu		
100	105	110
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly		
115	120	125
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu		
130	135	140
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala		
145	150	155
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr		
165	170	175
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu		
180	185	190
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu		
195	200	205
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly		
210	215	220
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His		
225	230	235
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu		
245	250	255
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg		
260	265	270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe		
275	280	285

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
 290 295 300
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
 305 310 315 320
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
 325 330 335
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
 340 345 350
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
 355 360 365
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
 370 375 380
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
 385 390 395 400
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
 405 410 415
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
 420 425 430
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
 435 440 445
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser
 450 455 460
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
 465 470 475 480
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 485 490 495
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
 500 505 510
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
 515 520 525
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
 530 535 540
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala
 545 550

<210> 114
 <211> 241
 <212> PRT
 <213> Homo sapien

<400> 114
 Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
 1 5 10 15
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
 20 25 30
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35 40 45
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50 55 60
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65 70 75 80
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Ile
 85 90 95
 Phe Ile Ala Glu Val Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

130	135	140													
Lys	Gly	Leu	Lys	Cys	Cys	Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp
145				150					155				160		
Ser	Pro	Tyr	Phe	Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn
							165		170				175		
Asp	Asn	Val	Thr	Asn	Thr	Ala	Asn	Glu	Thr	Cys	Thr	Lys	Gln	Lys	Ala
							180		185				190		
His	Asp	Gln	Lys	Val	Glu	Gly	Cys	Phe	Asn	Gln	Leu	Leu	Tyr	Asp	Ile
							195		200				205		
Arg	Thr	Asn	Ala	Val	Thr	Val	Gly	Gly	Val	Ala	Ala	Gly	Ile	Gly	Gly
							210		215				220		
Leu	Glu	Leu	Ala	Ala	Met	Ile	Val	Ser	Met	Tyr	Leu	Tyr	Cys	Asn	Leu
							225		230				235		
															240
															Gln

<210> 115
 <211> 366
 <212> DNA
 <213> Homo sapien

<400>	115					
gctctttctc	tccccccttc	tgaatttaat	tctttcaact	tgcaatttgc	aaggattaca	60
catttcactg	tgatgttat	tgtgttgcaa	aaaaaaaaaa	gtgtctttgt	ttaaaattac	120
ttgggtttgtg	aatccatctt	gtttttccc	cattggaaact	agtcattaac	ccatctctga	180
actggtagaa	aaacatctga	agagctagtc	tatcagcatc	tgacaggtga	attggatgg	240
tctcagaacc	atttcaccca	gacagcctgt	ttctatccgt	ttaataaaat	tagttgggt	300
tctctacatg	cataacaaac	cctgctccaa	tctgtcacat	aaaagtctgt	gacttgaagt	360
tttagc						366

<210> 116
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G

<400>	116					
acaaagatga	accatccct	atattatagc	aaaattaaaa	tctaccgta	ttctaatatt	60
gagaatgat	atnaaacaca	atnttataaa	gtctacttag	agaagatcaa	gtgacctcaa	120
agactttact	atttcatat	tttaagacac	atgatttac	ctattttagt	aacctgggtc	180
atacgtaaa	caaaggataa	tgtgaacacg	agagaggatt	tgttggcaga	aaatctatgt	240
tcaatctnga	actatctana	tcacagacat	ttctatcc	tt		282

<210> 117
 <211> 305
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(305)
 <223> n = A,T,C or G

<400> 117

acacatgtcg cttcaactgcc ttcttagatg cttctggtca acatanagga acagggacca	60
tattttatcct cccttcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa	120
aataaggcaa aatatatgaa acaacaggc tcgagatatt ggaaatcagt caatgaagga	180
tactgatccc tgcactgt cctaattgcag gatgtggaa acagatgagg tcacctctgt	240
gactgccccca gcttactgcc tgttagagagt ttctangctg cagttcagac agggagaaat	300
ttgggt	305
<210> 118	
<211> 71	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(71)	
<223> n = A,T,C or G	
<400> 118	
accacagggtgt ntgaatctct gacgtggga tctctgattc ccgcacaatc tgagtggaaa	60
aantccctggg t	71
<210> 119	
<211> 212	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(212)	
<223> n = A,T,C or G	
<400> 119	
actccgggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca	60
gaaaatgggg taaaattggc caacttctta tnaactttag ttggcaantt tgccaccaac	120
agtaagctgg cccttctaataaaaagaaaat taaaagggtt ctcactaanc ggaattaant	180
aatggantca aganactccc aggccctcagc gt	212
<210> 120	
<211> 90	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(90)	
<223> n = A,T,C or G	
<400> 120	
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggtcttgcc	60
ctccggccggc gcagaacatg ctgggggtgt	90
<210> 121	
<211> 218	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	

<222> (1) . . . (218)
 <223> n = A,T,C or G

<400> 121
 tgtancgtga anacgacaga nagggttgc aaaaatggag aanccttcaa gtcattttga 60
 gaataagatt tgctaaaaga tttggggcta aaacatggtt attgggagac atttctgaag 120
 atatncangt aaattangga atgaattcat ggttctttt ggaattcctt tacgatngcc 180
 agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122
 <211> 171
 <212> DNA
 <213> Homo sapien

<400> 122
 taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaaagg 60
 catttgttag ctcatggAAC aggaagtCGG atgggtgggc atcttcagtG ctgcattgAGT 120
 caccACCCG gcggggTCAT ctgtGCCACA ggtccCTGTT gacagtGCGG t 171

<210> 123
 <211> 76
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) . . . (76)
 <223> n = A,T,C or G

<400> 123
 tgttagcgtga agacnacaga atgggtgtg ctgtgctatC caggaacaca tttattatca 60
 ttatcaanta ttgtgt 76

<210> 124
 <211> 131
 <212> DNA
 <213> Homo sapien

<400> 124
 acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt 60
 caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctttgg 120
 ttaagatttG t 131

<210> 125
 <211> 432
 <212> DNA
 <213> Homo sapien

<400> 125
 acttttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg 60
 cttggaaaag aggtgatagc tcttcagagg acttgtact tttgctcaga tgctgaagaa 120
 ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagGA tgctgaagat 180
 ttgcctcacc aaacaaaagt gaaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240
 ctcttgaagt atcagtcact tttgagaatG tttcttagtt actgcatact tcattggatcc 300
 catgggtgggg gtcttgcattc tgtaagaatG gaattgatTT tgctttgca agaatctcg 360
 cagggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc 420
 ctctttgctt gt 432

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<210> 126
<211> 112
<212> DNA
<213> Homo sapien

<400> 126
acacaacttg aatagtaaaa tagaaaactga gctgaaattt ctaattcaact ttctaaccat      60
agtaagaatg atatccccc ccagggatca ccaaataattt ataaaaattt gt                112

<210> 127
<211> 54
<212> DNA
<213> Homo sapien

<400> 127
accacgaaac cacaaacaag atggaagcat caatccactt gccaaagcaca gcag            54

<210> 128
<211> 323
<212> DNA
<213> Homo sapien

<400> 128
acctcattag taattgtttt gttgtttcat tttttctaa tgtctccctt ctaccagctc      60
acotgagata acagaatgaa aatggaagga cagccagatt tctccttgc tctctgtca      120
ttctctctga agtcttaggtt acccattttg gggaccatt ataggcaata aacacagttc      180
ccaaagcatt tggacaggtt ctttgtgtgt tttagaatgg ttttcccttt tcttagcctt      240
ttcctgaaa aggctcaactc agtcccttgc ttgctcagtg gactgggctc cccagggcct      300
aggctgcctt ctttccatg tcc                323

<210> 129
<211> 192
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(192)
<223> n = A,T,C or G

<400> 129
acatacatgt gtgtatattt ttaaatatca cttttgtatc actctgactt ttttagcatac      60
tggaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcata      120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg      180
gataaaacaaa gt                192

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(362)
<223> n = A,T,C or G

<400> 130
cccttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctcttgaca      60

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tataatgacg caacaaaaag gtgctgttta gtcctatgg tcaagtttatg cccctgacaa	120
gtttccattg tggtttgcgg atcttctggc taatcggtt atcctccatg ttattagtaa	180
ttctgtattc cattttgtt aacgcctggta gatgtAACCT gctangaggc taactttata	240
cttatTTaaa agctttatt ttgtgtcat taaaatggca atttATGTGc agcactttat	300
tgcagcagga agcacgttg ggTTGGTTgt aaagctttt gctaattttt aaaaAGTAATG	360
gg	362
<210> 131	
<211> 332	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(332)	
<223> n = A,T,C or G	
<400> 131	
ctttttgaaa gatcggtgtcc actccctgtgg acatcttgg ttaatggagt ttcccattgca	60
gtangactgg tatgggttgcg gctgtccaga taaaacatt tgaagagctc caaaatgaga	120
gttctcccaag gttcggccctg ctgctccaag ttcagcggc acgcctttt aggaggcattc	180
ttctgtacta gattaaggca gcttggaaat ctgtatgtat ttgggttattt atccaactaa	240
cttcattctg ttatcactgg agaaAGCCCA gactccccan gacnggtacg gattgtggc	300
atanaaggat tgggtgaagc tggcgttgg	332
<210> 132	
<211> 322	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(322)	
<223> n = A,T,C or G	
<400> 132	
acttttgcca ttttgtatataaaacaatc ttgggacatt ctccgtaaaaa ctaggtgtcc	60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccaggcat gacacagaat	120
ctcaaattcc caaacagggg ctctgtgggaaaatgaggg aggacctttg tatctcggtt	180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagatgg	240
ggatgtttct aaaaaaaaaact ttggtagaga aaattaggaat gctnaatcct agggaaaccc	300
gtaacaatct acaattggtc ca	322
<210> 133	
<211> 278	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(278)	
<223> n = A,T,C or G	
<400> 133	
acaaggccttc acaagttttaa ctaaaattggg attaatcttt ctgtantttt ctgcataatt	60
cttgggttttc tttccatctg gtcctgggt tgacaatttg tggaaacaac tctattgtca	120
ctatTTaaa aaaatcacaa atcttccct ttaagctatg ttnaattcaa actattcctg	180
ctattcctgt tttgtcaaag aaattatatt tttcaaaaata tgtntattt tttgtatgggt	240

cccacgaaac actaataaaa accacagaga ccagcctg	278
<210> 134	
<211> 121	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(121)	
<223> n = A,T,C or G	
<400> 134	
gtttnaaaaa cttgttttagc tccatagagg aaagaatgtt aaactttgtta ttttaaaaaca	60
tgattctctg aggttaaact tggtttcaa atgttatttt tacttgtatt ttgttttgg	120
t	121
<210> 135	
<211> 350	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(350)	
<223> n = A,T,C or G	
<400> 135	
acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc	60
atancaagtgt gtagctgggtt aagcgctgcga caaagggtcag ctggcacatt acttgtgtgc	120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggn tggtaactcca	180
gggtgcggccc caactcctgc agccgctct ctgtgccagn ccctgnaagg aactttcgct	240
ccacctcaat caagccctgg gccatgtac ctgcaattgg ctgaacaaac gtttgctgag	300
tteccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt	350
<210> 136	
<211> 399	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(399)	
<223> n = A,T,C or G	
<400> 136	
tgtaccgtga agacgacaga agttgcattt cagggacagg gcagggccga ggccagggtt	60
gctgtgattt tatccgataa ntccctcggtga gaaaagataa tgagatgacg tgagcagcct	120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgccc ttggctctga	180
cctggcgccc agccagccag ccacaggtgg gcttcttctt ttgtgggtga caacnccaag	240
aaaactgcag aggccccaggg tcaggtgtta gtgggtangt gaccataaaa caccaggtgc	300
tcccaggaac cccggcaaaag gccatccccca cctacagcca gcatgccac tggcgtgatg	360
ggtgcagang gatgaagcag ccagntgttc tgctgtgg	399
<210> 137	
<211> 165	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(165)
<223> n = A,T,C or G

<400> 137
actggtgtgg tngggggtga tgctgggtgtt anaagttgan gtgacttcan gatgggtgtt      60
ggaggaagtg tgtgaacgta gggatgtaga nttttggcc gtgctaaatg agcttcggga      120
ttggctggtc ccaactgggtt tcactgtcat tggtgggtt cctgt      165

<210> 138
<211> 338
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(338)
<223> n = A,T,C or G

<400> 138
actcaactggaa atgccacatt cacaacagaa tcagaggctt gtgaaaacat taatggctcc      60
ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccac      120
tgctggcag tctccatgc cttccacagt gaaaggctt gagaaaaatc acatccaatg      180
tcatgtttt ccagccacac caaaagggtgc ttgggtggaa gggctgggg catananggt      240
cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa      300
aaaaactgat gcctttttt tttttttt taaaattc      338

<210> 139
<211> 382
<212> DNA
<213> Homo sapien

<400> 139
gggaatcttg gttttggca tctggtttgc ctatagccga ggccactttt acagaacaaa      60
gaaaggact tcgagtaaga aggtgattt cagccagcc agtgcggaa gtgaaggaga      120
atccaaacag acctcgatcat tcctgggtgtt agccctggctg gtcaccgcc tattatctgc      180
atggccta ctcagggtct accggactct ggccccctgat gtctgttagtt tcacaggatg      240
ccttattgt cttctacacc ccacaggggcc ccctacttct tcggatgtt tttataataat      300
gtcagctatg tgccccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg      360
gcctggaact tgtttaaatgt      382

<210> 140
<211> 200
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(200)
<223> n = A,T,C or G

<400> 140
accaaancatt ctttctgttg tgtnngatt tactataggg gtttngctt ttctaaanat      60
acttttcatt taacancttt tgtaagtgt caggctgcac tttgtccat anaattattg      120
ttttcacatt tcaacttgc tttgtttgtc tcttanagca ttggtaaat cacatattt      180
atattcagca taaaggagaa      200

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<210> 141
<211> 335
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(335)
<223> n = A,T,C or G

<400> 141
actttatccc caaaaacactc atatgttgc aaaaaacacat agaaaaataa agtttggtgg      60
gggtgctgac taaaacctaa gtcacagact tttatgtgac agattggagc agggtttgg      120
atgcatgttag agaacccaaa ctaatttttt aaacaggata gaaacaggct gtctgggtga      180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg      240
tttttctacc agttcagaga tnggtaatg actantcca atggggaaaa agcaagatgg      300
attcacaaac caagtaattt taaacaaaga cactt      335

<210> 142
<211> 459
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(459)
<223> n = A,T,C or G

<400> 142
accaggttaa tattgccaca tatataccttt ccaattgcgg gctaaacaga cgtgtattta      60
gggtgttta aagacaaccc agcttaatat caagagaaaat tgtgacccctt catggagtat      120
ctgtatggaga aaacactgag tttgacaaa tcttattttt ttcagatagc agtctgtatca      180
cacatggtcc aacaacactc aaataataaa tcaaataatna tcagatgtt aagattggtc      240
ttcaaaacatc atagccaatg atgccccgt tgccctataat ctctccgaca taaaaccacca      300
tcaacacccctc agtggccacc aaaccattca gcacagcttc ctttaactgtg agctgtttga      360
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaataagct cttagggatct      420
cagcanggggt gggaggaacc agctcaacct tggcgtant      459

<210> 143
<211> 140
<212> DNA
<213> Homo sapien

<400> 143
acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg      60
aaatccaaac agtctctcct agaaaggaat agtgtcacca acccccaccca tctccctgag      120
accatccgac ttccctgtgt      140

<210> 144
<211> 164
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(164)
<223> n = A,T,C or G

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<pre> <400> 144 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatctt gtcatttct 60 atctatacca ctctcccttc tgaaaacaan aatcaactanc caatcaactta tacaaatttg 120 aggcaattaa tccatatttgc ttcaataa ggaaaaaaag atgt 164 <210> 145 <211> 303 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(303) <223> n = A,T,C or G <400> 145 acgttagacca tccaaactttg tatttgaat ggcaaacatc cagnagcaat tcctaaacaa 60 actggagggt atttataccc aattatcccc ttcattaaca tgccctccctc ctcaggctat 120 gcaggacagc tatacataagt cggcccgaggc atccagatac taccatttgt ataaacttca 180 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240 tagtaaaatn ttgcttagt gaaacagcca caaaagactt accgccgtgg tgattaccat 300 caa 303 <210> 146 <211> 327 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(327) <223> n = A,T,C or G <400> 146 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60 actggcctgg agtgactcat tgctctgggt ggttgagaga gtcctttgc caacaggcct 120 ccaaagtcaagg gctgggattt gtttccttgc cacattctag caacaatatg ctggccactt 180 cctgaacagg gaggggtggga ggagccagca tggaaacaaggc tgccacttgc taaagttagcc 240 agacttgccc ctgggcctgt cacacactt gatgaccccttgc tggcctgca ggatggaatg 300 taggggtgag ctgtgtgact ctatgt 327 <210> 147 <211> 173 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(173) <223> n = A,T,C or G <400> 147 acattgtttt ttttagataa agcattgana gagctcttcc tAACGTGACA caatggagg 60 actggAACAC atacccacat ctttggctgt agggataatt ttctgataaa gtcttgctgt 120 atattcaac acatatgtt tatattttc agttccatgt ttatagccca gtt 173 <210> 148 </pre>	
---	--

<211> 477
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(477)
 <223> n = A,T,C or G

<400> 148

acaaccactt tatctcatcg aatttttaac ccaaactcac tcactgtgcc tttctatcct	60
atgggatata ttatgtatg ctccatttca tcacacatat atgaataata cactcatact	120
gccctactac ctgctgcaat aatcacattc ctttcctgtc ctgaccctga agccattggg	180
gtggctctag tggccatcag tccangcctg caccttgagc cctttagtgc cattgctcac	240
ccancccac ctcaccgacc ccatcctctt acacagctac ctcttgctc tctaacccca	300
tagattatnt ccaaattcag tcaattaagt tactattaac actcttacccg acatgtccag	360
caccactggt aaggcttctc cagccaacac acacacacac acacncacac acacacat	420
ccaggcacag gctacacctat cttcacaatc acccctttaa ttaccatgtc atgggtgg	477

<210> 149
 <211> 207
 <212> DNA
 <213> Homo sapien

<400> 149

acagttgtat tataatatac agaaataaac ttgcaatgag agcatttaag aggaaagaac	60
taacgttatt tagagagcca aggaaggaaa ctgtggggag tggatgtaa ggtggggcct	120
gtatataat aagagtcaac cagtaagtg ggtgtgtgg tatggcaca gtgaagaaca	180
ttcaggcag aggaaacac agtggaaa	207

<210> 150
 <211> 111
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(111)
 <223> n = A,T,C or G

<400> 150

accttgattt cattgctgct ctgatggaaa cccaactatac taatggatct aaaacatggg	60
cacttaatgt tggtcagttt ttggacttgt taactantgg catctttggg t	111

<210> 151
 <211> 196
 <212> DNA
 <213> Homo sapien

<400> 151

agcgccggcag gtcatttgc acattccaga tacctatcat tactcgatgc tggataac	60
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tggaaaaccat	120
ggataccaac cggaaaaccc cttatcccgc cagcccactg tggccccac tgtctacgag	180
gtgcattccgg ctcagt	196

<210> 152
 <211> 132
 <212> DNA

<213> Homo sapien

<400> 152
acagcacctt cacatgttaag aagggagaaa ttccctaaatg taggagaaaag ataacagaac 60
cttccccctt tcatctagt gttggaaacct gatgtttat gttgacagga atagaaccag 120
gaggaggttt gt 132

<210> 153
<211> 285
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(285)
<223> n = A,T,C or G

<400> 153
acaanaccca nganaggcca ctggccgtgg tgcataggcc tccaaacatg aaagtgtcag 60
cttcgtct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga 120
gcacatcaat aaagtccaaa gtcttgact tggccttggc ttggaggaaag tcatcaacac 180
cctggctagt gagggtgcgg cgccgcctct ggatgacggc atctgtgaag tcgtgcacca 240
gtctgcagggc cctgtggaaag cgccgtccac acggagtnag gaatt 285

<210> 154
<211> 333
<212> DNA
<213> Homo sapien

<400> 154
accacagtcc tggtggccca gggcttcatg accctttctg tgaaaagcca tattatcacc 60
accccaaatt ttcccttaaa tatcttaac tgaaggggtc agccttctga ctgcaaagac 120
cctaagccgg ttacacagct aactcccact gcccctgatt tgtgaaattt ctgtgcctg 180
attggcacag gagtcgaagg tggcctcgtc ccctcctcgg tggAACgaga ctctgatttg 240
agttcacaa attctcgggc cacctcgtca ttgctctct gaaataaaaat ccggagaatg 300
gtcaggcctg tctcatccat atggatctc cgg 333

<210> 155
<211> 308
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(308)
<223> n = A,T,C or G

<400> 155
actggaaaata ataaaaccca catcacagt gttgtcaaa gatcatcagg gcatggatgg 60
gaaagtgcctt tgggaaactgt aaagtgccta acacatgatc gatgatTTT gttataatat 120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tggggcccaag ccccaagcccc 180
atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt ctcttggct 240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtcta aggcatgctg 300
gccctgg 308

<210> 156
<211> 295
<212> DNA

<213> Homo sapien

<400> 156

```
accttgctcg gtgctggaa catatttagga actcaaaaata tgagatgata acagtgccta      60
ttattgatta ctgagagaac ttttagacat ttgttgaag atttctaca caggaactga      120
gaataggaga ttatgttgg ccctcatatt ctctcctatc ctccctgcct cattctatgt      180
ctaataatatt ctcaatcaa taaggttagc ataatcagga aatcgaccaa ataccaatat      240
aaaaccagat gtctatcctt aagatttca aatagaaaac aaattaacag actat      295
```

<210> 157

<211> 126

<212> DNA

<213> Homo sapien

<400> 157

```
acaagtttaa atagtgttgt cactgtgcat gtgctgaaat gtgaaatcca ccacattct      60
gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtggta tatctgtccc      120
cttagt      126
```

<210> 158

<211> 442

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(442)

<223> n = A,T,C or G

<400> 158

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acccactggt ctggaaaca cccatccta atacgatgat ttttctgtcg tggaaaatg      60
aanccagcg gctcccccta gtcagtcctt cttccagag aaaaagagat ttgagaaagt      120
gcctggtaa ttcaccatc atttctccc ccaaactctc tgagtcttcc cttaatattt      180
ctggtggttc tgaccaaagc aggtcatggt ttgtttagca tttggatcc cagtgaaatg      240
natgtttgtc gccttcata cttagccctt cccacgcaca aacggagtgg cagagtgg      300
ccaaacctgt tttccagtc cacgtagaca gattcacatg gcgaaattct ggaagctgga      360
nacagacggg ctctttgcag agccggact ctgagangga catgagggcc tctgcctctg      420
tgttcattct ctgatgtcct gt      442
```

<210> 159

<211> 498

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(498)

<223> n = A,T,C or G

<400> 159

```
acttccaggt aacgttgggg tttccgttga gcctgaactg atgggtgacg ttgttaggttc      60
tccaaacaaga actgagggtt cagagccgggt agggaaagagt gctgttccag ttgcacctgg      120
gctgctgtgg actgttgggg attcctcaact acggcccaag gttgtggaaac tggcanaaag      180
gtgtgttgtt gganttgagc tcggggggct gtggtaggtt gtgggcttt caacaggggc      240
tgctgtgggg cccggggatgtt aangtgggg tgcacttgg cttggccacg tctggaaatg      300
antanattct tcctgaaggc cagegttggt ggagctggca ngggtcantg ttgtgtgtaa      360
cgaaccatgt ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatgtgtcn      420
tcaggtaana atgtgggttc agtgccttggcngctgtg gaaggttga nattgtcacc      480
```

aagggaataa gctgtggt	498
<210> 160	
<211> 380	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(380)	
<223> n = A,T,C or G	
<400> 160	
acctgcatcc agcttccctg ccaaactcac aaggagacat caacccttag acagggaaac	60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaaatat tcccatgcct	120
ggagcatggc atagaggaag ctgaaaatg tgggtctga ggaagccatt tgagtctggc	180
cactagacat ctcatcagcc acttgtgtga agagatgcc catgaccca gatgcctctc	240
ccacccttac ctccatctca cacactttag cttccactc tgtataattc taacatcctg	300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggtt gaggctgatt tctaacgaaa	360
ctttagaat gaagcctgga	380
<210> 161	
<211> 114	
<212> DNA	
<213> Homo sapien	
<400> 161	
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatggcc ttgcctgtca	60
cactgtccac tggccctta tccacttgtt gcttaatccc tcgaaagagc atgt	114
<210> 162	
<211> 177	
<212> DNA	
<213> Homo sapien	
<400> 162	
actttctgaa tcgaatcaaa tgatacttag tggatttta atatcctcat atatataaaa	60
gttttactac tctgataatt ttgtaaacca ggttaaccaga acatccagtc atacagcttt	120
tggatata taacttggca ataaccaggc atgggtgatac ataaaactac tcactgt	177
<210> 163	
<211> 137	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(137)	
<223> n = A,T,C or G	
<400> 163	
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtagc	60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt	120
catcagggc atgatgt	137
<210> 164	
<211> 469	
<212> DNA	

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatacacaa tgaatgttct cctgggcagc gttgtgatct ttgccacatt cgtgacttta	60
tgcataatgcatt catgctattt cataacctaat gagggagttc caggagattc aaccaggaaa	120
tgcatggatc tcaaaggaaa caaacaccca ataaaactcg agtggcagac tgacaactgt	180
gagacatgca cttgtctacga aacagaaaatt tcatgttgca cccttgttc tacacctgtg	240
ggttatgaca aagacaactg ccaaagaatac ttcaagaagg aggactgcaa gtatatcgtg	300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct	360
tcttagtagc acagggcctcc caggccaggc ctcattctcc tctggcctct aatagtcaat	420
gattgtgttag ccatgcctat cagtaaaaag atntttgagc aaacacttt	469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt atanataatcg acattgccgg cacttgggtt cagtttcata aagctgggtgg	60
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatacg cccatgtccc	120
tgcaaggccgc ccggcccttag ttctcggtcc agtctgtttt gcacacaggg tgccaggact	180
tcctctgaga tgagt	195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcg	60
cgagggtcggaa gtccacacca ccgggtttagg tgtgtcaat ctgggttgc gcccacat	120
ttggagaagg gatatgtgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt	180
tttcagacc agcttgagca agggccggat gtcagttc agtctcttgc tcgtcagggt	240
gatgcacacc tcgtctangg tccgtggaa gctgggttcc acntcaccta caacctgggc	300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgttagt	360
nggggccttt ttggtaact ttc	383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

```

<221> misc_feature
<222> (1)...(247)
<223> n = A,T,C or G

<400> 167
acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtgcgat 60
tggagcagaa actggagcaa gaagtggcc tggggctgaa gtagagacca aggccactgc 120
tatancata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180
tcaatctgan tccaaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240
tgangtc 247

<210> 168
<211> 273
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(273)
<223> n = A,T,C or G

<400> 168
acttctaagt tttctagaag tggaggatt gtantcatcc taaaaatggg tttacttcaa 60
aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg 120
gctgacacct gaggctgnat tttcactcat ccctgagaag ccctttccag tagggtgtggc 180
aattcccaac ttcttgcca caagctcccc aggcttctc ccctggaaaa ctccagcttg 240
agtcccagat acactcatgg gctgccctgg gca 273

<210> 169
<211> 431
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(431)
<223> n = A,T,C or G

<400> 169
acaggccttgg ctcccccaaa ctcccacagtc tcagtgcaga aagatcatct tccagcagtc 60
agctcagacc agggtcaaag gatgtgacat caacagttc tggtttcaga acaggttcta 120
ctactgtcaa atgacccccc atacttcctc aaaggctgtg gtaagtttg cacaggtgag 180
ggcagcagaa agggggtant tactgtgga caccatttc tctgtatact ccacactgac 240
cttgcctatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc 300
acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaaactgg 360
aaagtgatct gatactggat tcttaattac cttcaaaaagc ttctggggc catcagctgc 420
tcgaacactg a 431

<210> 170
<211> 266
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(266)
<223> n = A,T,C or G

```

<400> 170
 acctgtggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc 60
 tcaaggagct ctgcaggcat tttgccaanc ctctccanag canagggagc aacctacact 120
 ccccgcctaga aagacaccag attggagtcc tgggaggggg agttgggtg ggcatttgat 180
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240
 tcaaagctag gggctggca ggtgga 266

<210> 171
 <211> 1248
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1248)
 <223> n = A,T,C or G

<400> 171
 ggcagccaaa tcataaaacgg cgaggactgc agcccgcaact cgcagccctg gcaggcggca 60
 ctggcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcattcgca gtgggtgtg 120
 tcagccgcac actgtttcca gaagttagtgc cagagctcct acaccatcgg gctggccctg 180
 cacagtcttgc aggccgacca agagccagg agccagatgg tggaggccag cctctccgt 240
 cggcaccctg agtacaacag acccttgctc gctaacgacc tcatgtcat caagttggac 300
 gaatccgtgt ccgagtcgtga caccatccgg agcatcagca ttgcttcgca gtgccttacc 360
 gcgggaaact cttgcctctgt ttctggctgg ggtctgtctgg cgaacggcag aatgcctacc 420
 gtgtgtcagt gctgtgaacgt gtctgggtgt tctgaggagg tctgcagtaa gctctatgac 480
 ccgcgttacc acccccagat gttctgcgc ggcggaggc aagaccagaa ggactcctgc 540
 aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tttgtctttc 600
 ggaaaagccc cgtgtggcca agttggctgtcc ctaggtgttca acaccaacat ctgcaaatc 660
 actgagtggta tagagaaaac cgtccaggcc agttaactct ggggactggg aaccatgaa 720
 attgaccccc aaatacatcc tgctggaaaggat attcaggaat atctgttccc agcccttcc 780
 ccctcaggcc caggagtcca gggcccccagc ccctccccc tcaaaccat ggtacagatc 840
 cccagccctt cctccctcaag acccaggagt ccagaccccc cagcccttcc tccctcagac 900
 ccaggagtcc agcccttcc ccttcagacc caggagtcca gaccccccag ccctccccc 960
 ctcagaccca ggggtccagg ccccaaccc ctcctccctc agactcagag gtccaagccc 1020
 ccaaccntc attccccaga cccagaggc caggtcccag cccctcntcc ctcagaccca 1080
 gcggtccaaat gccacctaga ctntccctgt acacagtgcc cccttgc acgttgaccc 1140
 aaccttacca gttggttttt cattttngt cccttcccc tagatccaga aataaaat 1200
 aagagaagng caaaaaaaaaaaaaaaa aaaaaaaaaaaa aaaaaaaaaa 1248

<210> 172
 <211> 159
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(159)
 <223> Xaa = Any Amino Acid

<400> 172
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1 5 10 15
 Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
 20 25 30
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
 35 40 45
 Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

50	55	60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu		
65	70	75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe		80
85	90	95
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser		
100	105	110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe		
115	120	125
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn		
130	135	140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser		
145	150	155

<210> 173

<211> 1265

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1265)

<223> n = A,T,C or G

<400> 173

ggcagccgc actcgagcc ctggcaggcg gcactggtca tggaaaacga attgttctgc	60
tccggcgtcc tggtgcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc	120
tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg	180
gtggaggcca gccttcgtt acggcaccca gagtacaaca gaccctgtct cgctaacgc	240
ctcatgctca tcaagtttggc cgaatccgtg tccgagtctg acaccatccg gagcatcagc	300
attgttctgc agtgcctac cgccccaaac tcttgcctcg ttctggctg gggctgtctg	360
gcgaacggtg agctcacggg tgggtgtctg ccctcttcaa ggaggccctc tgcccagtc	420
cggggctgaa cccagagctc tgcgtccctcg gcagaatgcc taccgtctg cagtgcgtga	480
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgaccgcgtg taccacccca	540
gcatgttctg cgccggcgaa gggcaagacc agaaggactc ctgcaacggg gactctgggg	600
ggccctgtat ctgcaacggg tacttgccagg gccttgcgtc ttctggaaaa gcccgtgtg	660
gcgaagtgg cgtgcctcg gtctacacca acctctgcaaa attactgag tggatagaga	720
aaaccgttcca ggccagttaa ctctggggac tggaaaccca tgaatttgc cccaaatac	780
atccctgcggaa aggaattttagt gaatatctgt tcccgcccccc tccctccatca ggcccaggag	840
tccaggcccc cagccccctcc tccctcaaacc caagggtaca gatccccccgc ccctccctcc	900
tcagaccccgagatcccgac ccccccggccctc ctccctccctc agacccaggaa gtcccgcccc	960
tcctccntca gaccggccaggat tccagcccccc ccaccccccctc ctccctcaga cccagggggtt	1020
gaggccccca accccctccctc ttccagatgc agagggtccaa gcccccaacc cctcggtcccc	1080
cagacccaga gtnnnaggtc ccagccccctc ttccntcaga cccagnggtc caatgccacc	1140
tagattttcc ctgnacacag tggccccctt tgnangttt acccaacctt accagtttgt	1200
tttcatttt tngtcccttt cccctagatc cagaaataaaa gtttaagaga ngngcaaaaa	1260
aaaaaa	1265

<210> 174

<211> 1459

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1459)

<223> n = A,T,C or G

<400> 174

ggtcagccgc acactgttgc cagaagttag tgcagagctc ctacaccate gggctgggccc	60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agccctctccg	120
tacggcaccc agagtacaac agacccttgc tcgctaacga cctcatgctc atcaagttgg	180
acgaatccgt gtcccgagtct gacaccatcc ggagcatcag cattgttgc cagtgcctaa	240
ccgcggggaa ctcttgctc gtttctggct ggggtctgt ggcgaacggg gagctcaegg	300
gtgtgtgtct gccccttca aggaggtcct ctgcccagtc gcgggggctg acccagagct	360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tgggtgtctga	420
ngaggtctgc antaagctct atgaccggct gtaccacccc ancatgttct gcgcggcgg	480
aggcgaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact	540
cagggaaaggg tggagaaggg ggagacagag acacacaggg ccgcataggc agatgcagag	600
atggagagac acacagggag acagtgcacaa cttagagagag aaactgagag aacacagagaa	660
ataaacacag gaataaaagag aagcaaagga agagagaaaac agaaacagac atggggaggc	720
agaaacacac acacatagaa atgcagtta ctttccaaca gcatggggcc tgagggcggt	780
gacctccacc caatagaaaa tcctttata acttttgact ccccaaaaac ctgactagaa	840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgatatt atgcatacg	900
tttatgcatt catgatatac ctttgttga atttttgat atttctaagc tacacagttc	960
gtctgtgaat tttttaaat tggttcaact ctcctaaaat ttttctgtat tggttattga	1020
aaaaatccaa gtataagtgg acttgcacat tcaaaaccagg gttgttcaag ggtcaactgt	1080
gtacccagag gggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa	1140
aaatcaagac tctacaaaaga ggctgggcag ggtggctcat gcctgtatac ccagcacttt	1200
gggaggcgg gcaaggcagat cacttgaggt aaggagttca agaccaggct ggc当地atg	1260
gtggaaatct gtctgtacta aaaatacaaa agtttagctgg atatggggc agggccctgt	1320
aatcccgat acttggggg ctgaggcagg agaattgtctt gaatatggga ggc当地aggtt	1380
gaagttagtt gagatcacac cactatactc cagctgggc aacagagtaa gactctgtct	1440
aaaaaaaaaaaa aaaaaaaaaaaaa	1459

<210> 175

<211> 1167

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1167)

<223> n = A,T,C or G

<400> 175

gcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgtc gggcgccctg	60
gtgcacccgc agtgggtgt gtcagccgca cactgttcc agaactccta caccatcgaa	120
ctggccctgc acagtcttgc ggccgaccaa gagccaggaa gccagatggt ggaggccagc	180
ctctccgtac ggcacccaga gtacaacaga ctcttgcctg ctaacgaccc catgtctatc	240
aagtggacg aatccgtgtc cgagtcgtac accatccggaa gcatcagcat tgcttcgcag	300
tgcccttaccg cggggaaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga	360
atgccttaccg tgctgtactg cgtgaacgtg tcgggtgtgt ctgaggangt ctgcagtaag	420
ctctatgacc cgctgtacca ccccaacatg ttctgcgcgg gcggaggggca agaccagaag	480
gactctgtca acgggtgactc tggggggccc ctgatctgtca acgggtactt gcaggccctt	540
gtgttcttcg gaaaagcccc gtgtggccaa ctggcgctgc caggtgtcta caccaaccc	600
tgcaatttcg ctgagttggat agagaaaacc gtccagncca gttaaactctg gggactggga	660
acccatgaaa ttgaccccca aatacatctt gccaangaa ttcaagaaata tctgttccca	720
gccccctctc ctcaggcccc aggagtccag gccccccagcc ctcctccct caaaccagg	780
gtacagatcc ccaggccctc ctccctcaga cccaggagtc cagaccccccc agccctctt	840
ccntcagacc caggagtccca gccccctctc cntcagacgc aggagtccag accccccagc	900
ccntcntccg ttagggccag gggtgaggc ccccaacccc tntccntca gagtcagagg	960
tccaagcccc caacccctctc ttccccccagcc ccaagggtnc aggtccctcgc ccctccccc	1020
tcagacccag cgggtccaaatg ccacctagan ntccctgtca cacagtcccc ccttgtggca	1080
ngttgaccca accttaccag ttggtttttc atttttgc ctttccctt agatccagaa	1140
ataaaagnta agagaagcgc aaaaaaaaaaaaa	1167

<210> 176
<211> 205
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(205)
<223> Xaa = Any Amino Acid

<400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
1 5 10 15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
20 25 30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
35 40 45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu
50 55 60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65 70 75 80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
85 90 95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
100 105 110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
115 120 125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
130 135 140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
145 150 155 160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
165 170 175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
180 185 190
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
195 200 205

<210> 177
<211> 1119
<212> DNA
<213> Homo sapien

<400> 177

gcgcaactcgc agccctggca ggccggactg gtcatggaaa acgaattgtt ctgctcgccc	60
gtccctgggtgc atcccgactg ggtgtgtca gccgcacact gttccagaa ctccctacacc	120
atcgggctgg gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatgggtggag	180
gccagccctct ccgtacggca cccagagtc aacagaccct tgctcgtaa cgacctcatg	240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgtct	300
tcgcgtgtcc ctaccgggg gaactttgc ctcgtttctg gctgggtct gctggcgaac	360
gatgtgtga ttgccccatccca gtcccaactg gtggggaggct gggaggtgtga gaagctttcc	420
caaccctggc aggggttgtac catttcggca acttccagtg caaggacgtc ctgtgcata	480
ctcaactgggt gtcactact gtcactgtca tcacccggaa cactgtgtatc aacttagccag	540
caccatagtt ctccgaagtc agactatcat gattactgtt ttgactgtgc tgtctattgt	600
actaaccatg ccgatgttta ggtgaaattt ggtcaacttg gcctcaacca tcttggatcc	660
cagttatcct cactgaattt agatttcctg cttcagtgtc agccattccc acataatttc	720
tgacctacag aggtgaggga tcatatagct cttcaaggat gtcgtactc ccctcacaaa	780

ttcatttctc ctgtttagt gaaagggtgcg ccctctggag cctccaggg tgggtgtgca	840
ggtcacaatg atgaatgtat gatcggttc ccattacca aagccttaa atccctcatg	900
ctcagtacac cagggcaggt ctagcatttc ttcattttagt gtatgtgtc cattcatgca	960
accacctcg gactcctgga ttctctgcct agttgagctc ctgcgtgtc cctccttggg	1020
gaggtgaggg agagggccca tggtcaatg ggatctgtgc agttgtaca cattaggtgc	1080
ttaataaaaca gaagctgtga tgtaaaaaaa aaaaaaaaaa	1119

<210> 178
<211> 164
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1) . . . (164)
<223> Xaa = Any Amino Acid

<400> 178

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp			
1	5	10	15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu			
20	25	30	
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val			
35	40	45	
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu			
50	55	60	
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser			
65	70	75	80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly			
85	90	95	
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val			
100	105	110	
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu			
115	120	125	
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg			
130	135	140	
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser			
145	150	155	160
Pro Gly Thr Leu			

<210> 179
<211> 250
<212> DNA
<213> Homo sapien

<400> 179

ctggagtgcc ttgggtttc aagccctgc aggaaggaga atgcacccccc tgaggcacct	60
ccagctcccc ccggccgggg gatgcgaggc tcggagcacc cttggccggc tgtgattgct	120
gccaggact gttcatctca gctttctgt ccctttgtc ccggcaagcg cttctgtga	180
aagttcatat ctggagccctg atgtcttaac gaataaaggt cccatgtccc accggaaaaaa	240
aaaaaaaaaa	250

<210> 180
<211> 202
<212> DNA
<213> Homo sapien

<pre> <400> 180 actagtccag tgtgggtggaa ttccattgtg ttggggcccaa cacaatggct accttaaca tcacccagac cccgccccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta ctctgctact cgaaaaactat ttttatgtaa ttaatgtatg ctttcttgaa tataaatgcc tgataaaaaa aaaaaaaaaaa aa </pre> <pre> <210> 181 <211> 558 <212> DNA <213> Homo sapien </pre> <pre> <220> <221> misc_feature <222> (1)...(558) <223> n = A,T,C or G </pre> <pre> <400> 181 tccytttgkt naggtttkkg agacamccck agacctaann ctgtgtcaca gacttcyyngg aatgtttagg cagtgttgt aatttcytcg taatgattct gtttattactt tcctnattct ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaaa ggtagtgtga tagtataagt atctaagtgc agatgaaaat gtgttataata tatccattca aaattatgca agttagtaat tactcagggt taactaaatt actttaataat gctgttgaac ctactctgtt ctttggctag aaaaaattat aaacaggact ttgttagttt gggaaagccaa attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw ttttattccc aggaatatgg kgttcatttt atgaatatta cscrrgatag awgtwtgagt aaaaycagtt ttggwtwaata ygtwaatatg tcmtaaataaa acaakgtttt gacttatttc aaaaaaaaaa aaaaaaaaaa </pre> <pre> <210> 182 <211> 479 <212> DNA <213> Homo sapien </pre> <pre> <220> <221> misc_feature <222> (1)...(479) <223> n = A,T,C or G </pre> <pre> <400> 182 acagggwttk grggatgcta agsccccrga rwtygtttga tccaaccctg gcttwtttc agagggaaa atggggccctaa gaagttacag mscatyttagy tggtgcgmgt gcacccctgg cstcacacag astcccggat agctggact acaggcacac agtcaactgaa gcagggccctg ttwgcattt acgttggccac ctccaaacttta aacatttttcc atatgtatg tccttagtca ctaaggtaa actttccac ccagaaaagg caacttagat aaaatcttag agtactttca tactmttcta agtcctcttc cagcctcaact kkgagtcctm cytgggggtt gataggaant ntcttgc ttctcaata aartcttat ycatctcatg ttaatttgg tacgcatara awtgstgara aattaaaaat gttctggatty mactttaaaa araaaaaaaaaa aaaaaaaaaa </pre> <pre> <210> 183 <211> 384 <212> DNA <213> Homo sapien </pre> <pre> <400> 183 aggccggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc agtaccagta ccaataacag tgccagtgcc agtgcacca ccagtgggtt cttcagtgtct ggtgccagcc tgaccggccac tctcacattt gggcttctcg ctggccttgg tggagctgg gccagcacca gtggcagctc tggtgcctgt gtttcttcc acaagtgaga ttttagatat </pre>	60 120 180 202 60 120 180 202 60 120 180 240 300 360 420 480 540 558 60 120 180 240 300 360 420 480 540 558 60 120 180 240 300 360 420 480 540 558 60 120 180 240 300 360 420 480 540 558
---	--

tgtaatcct gccagtctt ctctcaagc cagggtcat cctcagaaac ctactcaaca	300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt	360
gccatttcaa aaaaaaaaaaaa aaaa	384
<210> 184	
<211> 496	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(496)	
<223> n = A,T,C or G	
<400> 184	
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aggagagatcg agtctatacg ctgaagaaat ttgaccggat gggacaacag acctgctcag	120
cccatcctgc tcggttctcc ccagatgaca aatactctsg acacccaatc accatcaaga	180
aacgcttcaa ggtgctcatg acccagcaac cgcgcctgt cctctgaggg tcccttaaac	240
tgtatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact ctteggactg	300
tgagccctga tgcctttttt ccagccatac tcttggcat ccagtctctc gtggcgattg	360
attatgcttg tgtgaggcaa tcatggtggc atcacccata aaggaaacac atttgacttt	420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst	480
aaaaaaaaaaa aaaaaa	496
<210> 185	
<211> 384	
<212> DNA	
<213> Homo sapien	
<400> 185	
gctggtagcc tatggcgkkgg cccacggagg ggctcctgag gccacgrac agtgacttcc	60
caagtatcyt ggcgscgtc ttctaccgtc cttacgtca gatcttcggg cagattcccc	120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcgag cccggcttct	180
ggcacacccc tcctggggcc caggcgggca cctgcgtctc ccagtatgca aactggctgg	240
tggtgctgtc ctcgtcatc ttctgtctcg tggccaacat cctgctggc aacttgctca	300
ttgcccattt cagttacaca ttggcaag tacaggca cagcgatctc tactggaaag	360
gcccacgtt accgcctcat ccgg	384
<210> 186	
<211> 577	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(577)	
<223> n = A,T,C or G	
<400> 186	
gagttagctc ctccacaacc ttgatgaggc cgtctgcagt ggcctctcgc ttcataccgc	60
tnccatgtc atactgtagg tttgcacca cytcctggca tcttggggcg gcntaatatt	120
ccagaaaact ctcaatcaag tcacgtcga taaaacctgt gggctggtc tgcgttccgc	180
tgggtgaa aggtatccc agaaggagtg ctgcgttcc cccacactt tgatgacttt	240
attgagtcga ttctgtcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac	300
cagccctatc atgcgttga mcgtgccc garcaccgag cttgtgtgg gggkkgaaat	360
ctcacccaga ttctgtcatgtt ccagagagcc gtggcaaaag acattgacaa actcgcccag	420
gtggaaaaag amcamctcct ggargtgctn ggcgcctctc gtcmtgttgg ggcagcgctw	480

tcctttgac acacaaacaa gtaaaggca tttcagccc ccagaaantt gtcatcatcc	540
aagatntcgc acagcaactna tccagttggg attaaat	577
<210> 187	
<211> 534	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(534)	
<223> n = A,T,C or G	
<400> 187	
aacatcttcc tgtataatgc tgtgtataat cgatccgatn ttgtctgstg agaatycatw	60
actkggaaaa gmaacattaa agcctggaca ctggattaa aattcacaat atgcaacact	120
ttaaacagtg tgtcaatctg ctccccynac ttgtcatca ccagtcgtgg aakaaggta	180
tgccttattc acacctgtta aaaggcgct aagcattttt gattcaacat ctttttttt	240
gacacaagtc cgaaaaaaagc aaaagtaaac agttatyat ttgttagcca attcactttc	300
ttcatgggac agagccatyt gataaaaaa gcaaattgca taatattgag cttygggagc	360
tgatatttga gcggaagagt agccttcta cttcaccaga cacaactccc ttcatattg	420
ggatgttnac naaagtwtatg tctctwacag atggatgct ttgtggcaa ttctgttctg	480
aggatctccc agtttattta ccacttgac aagaaggcgt tttcttcctc aggc	534
<210> 188	
<211> 761	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(761)	
<223> n = A,T,C or G	
<400> 188	
agaaaccagt atctctnaaa acaaccttc ataccttgc gacctaattt tggcgttg	60
tgtgtgtcg cgcatattat atagacaggc acattttt tactttgtt aaagcttatg	120
cctcttttgtt atctatatct gtgaaagtta taatgtctg ccataatgtc ttggggacct	180
ttgtcttcgtg tgtaaatggt actagagaaa acacctatnt tatgagtc aaactctcc	240
tttatttcgac atgaaggaaa ttccagatn acaacactna caaactctcc ctgackarg	300
ggggacaaag aaaagcaaaa ctgamataa raaacaatwa cctgggtgaga arttgataa	360
acagaaaatwr gtagtatata tgaarnacag catcattaaa rmgttwktt wttctccctt	420
gcaaaaaaca ttagcngact tcccggttag taatgccaag ttgtttttt tattataaaa	480
cttgccttc attacatgtt tnaaagtggt gtggggcc aaaatattga aatgatggaa	540
ctgactgata aagctgtaca aataagcgt gtgcctaaca agcaacacag taatgttgac	600
atgcttaatt cacaatgtc aatttcatta taaatgttg ctaaaataca ctttgaacta	660
ttttctgtt tcccagagc tgagatnta gatttatgt agtatnaagt gaaaaantac	720
gaaaataata acattgaaga aaaananaaa aaaaaaaaaa a	761
<210> 189	
<211> 482	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(482)	
<223> n = A,T,C or G	

<400> 189
ttttttttt tttgcgatn ctactatTTT attgcaggn gtgggggtgt atgcacccga 60
caccggggct atnagaagca agaaggaaagg agggaggcga cagcccttg ctgagcaaca 120
aagccgcctg ctgccttc tgcgtgtc tgggtgcagg cacatggga gaccttcccc 180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tggangtgt gcataagaag 240
tgataggcac agggcaccgg gtacagaccc ctcggctc tgcgtngt ttcgaccag 300
gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc ttccctttc 360
aaatttggct ngtcatngaa nggcanttt tccaantng gctnggtctt ggtacncttg 420
gttcggccca gtcnccgtc caaaaantat tcacccnnct ccnaattgtc tgcnngnccc 480
cc 482

<210> 190
<211> 471
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(471)
<223> n = A,T,C or G

<400> 190
ttttttttt ttttaaaaca gttttcaca aaaaaattt aatggatggat agtggtttg 60
aaaactctcg catccagtga gaactaccat acaccat acagctngga atgtntccca 120
aatgtctggt caaatgatac aatggAACCA tcaatctt cacatgcacg aaagaacaag 180
cgcttttgc atacaatgca caaaaaaaaaa agggggggggg gaccacatgg attaaaattt 240
taagtaactca tcacatacat taagacacag ttcttagtcca gtcnaaaatc agaactgcnt 300
tgaaaaattt catgtatgca atccaaaccaa agaacttnat tggtgatcat gantntcta 360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacnctgt acaaaaanaa 420
tctgtattn anttcaacct ccgtacngaa aaatnttnnt tatacactcc c 471

<210> 191
<211> 402
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(402)
<223> n = A,T,C or G

<400> 191
gagggattga aggtctgttc tattgtcggtt ctgttcagcc accaactcta acaagtgt 60
gtcttcact cactgtctgt aagtttttta acccagacwg tatcttcata aatagaacaa 120
atttttcacc agtcacatct tcttagaccc tttggattt agtttgtata agctttcca 180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgttagaaagg aattyattg 240
ctcggtctct aacaatgtcc ttccttgaa gtatttgct gaacaacccca cctaaagtcc 300
ctttgtgtcat ccattttaaa tataacttaat agggcatttgk tncactaggt taaattctgc 360
aagagtcatc tgcgtcaaaa agttgcgtt aatatctgc ca 402

<210> 192
<211> 601
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

<222> (1) ... (601)
 <223> n = A,T,C or G

<400> 192
 gagctcgat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact 60
 ggtctacccc acatgggagc agcatccgt agntatataa ggtcatccc tgagtcaagac 120
 atgcyyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccatccccyt 180
 ctttgtga aaaactggca ctktctgga actagcarga catcacttac aaattcaccc 240
 acgagacact taaaagggtt aacaaggcga ytcttgatt gcttttgc cctccggcac 300
 cagttgtcaa tactaaccgc ctggttgccc tccatcacat ttgtgatctg tagctctgga 360
 tacatctcct gacagtaactg aagaacttct tctttgttt caaaagcara tcttgggtgcc 420
 tggatca gttccatt tcccagtcyt aatgttcaca tggcatattt wacttccac 480
 aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattt gctgcaagag 540
 cctcgatgtt gccggccagc gccaaggcag ggcggctgag ccccaccagc agcagaagca 600
 g 601

<210> 193
 <211> 608
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (608)
 <223> n = A,T,C or G

<400> 193
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 ggtcccgctg tagccccagc gactctccac ctgctggaaag cggttgcattc tgcactcytt 120
 cccaaacgcag gcagmagcgg gscggtaaa tgaactccay tcgtggctt gggtkgacgg 180
 tkaagtgcag gaagaggctg accacccgcg ggtccaccag gatgcccac tgcggggac 240
 ctgcagcgaa actcctcgat ggtcatgacg ggaagcga tgaggcccac ggccttgcac 300
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 gaccagcggc caaacggcrt tgaacagccg cacccacgg atgcccactg tgcggcgtc 420
 caggammgscc accagcgtgt ccaggtaat gtccgtgaag ccctccgcgg gtratggcgt 480
 ctgcagtgtt ttgtcgatg ttctccaggc acaggctggc cagtcgcgtt tcatcgaaga 540
 gtcgcgcctg cgtgagcagc atgaaggcgt tgcggctcg cagtttttct tcaggaactc 600
 caccaat 608

<210> 194
 <211> 392
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (392)
 <223> n = A,T,C or G

<400> 194
 gaacggctgg accttgccctc gcattgtgt tgcgtggcagg gaatacctt gcaaggcagyt 60
 ccagtccgag cagccccaga ccgtgtccgc cccaagctaa gcctgcctt ggccttcccc 120
 tccgcctcaa tgcagaaccca gtatggggact cactgtgttt agatgtttaa gtaacactg 180
 tttgattttt cttggaaatt tcctctgttata tagtgcattt cccatgttta atttccaaac 240
 aacaacaaca aaataaacatg tttgcctgtt aagttgtata aaagtaggtt attctgtatt 300
 taaagaaaaat attactgttata cataactgc ttgcaatttgc tgtatttatt gkntnstgg 360
 aaataaaat agtttattaa ggttgcant cc 392

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<210> 195
<211> 502
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

<400> 195
ccsttkagg ggtkaggkyc cagttccga gtggaagaaa caggccagga gaagtgcgtg      60
ccgagcttag gcagatgttc ccacagtgc ccccaagagcc stgggstatt gtytctgacc    120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc    180
aaggaaaggc cccattccgg ggstgttccc cgaggaggaa gggaaaggggc tctgtgtgcc    240
ccccasgagg aagaggccct gagttctggg atcagacacc cttcacgtg tatccccaca    300
caaatgcaag ctccaagg tccctctca gtcccccttc stacaccctg amcgccact    360
gscscacacc caccagac acgcaccccg ccatggggar tgtgctcaag gartcgcnng    420
gcrcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt    480
gtnanaaaaaaa aaaaanaaaaaa aa                                         502

<210> 196
<211> 665
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(665)
<223> n = A,T,C or G

<400> 196
ggtaacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaaag ctttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt    120
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga    180
actwattttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkate    240
aagtatgatg aaaagcaawa gatatattt cttttattt gttaaattat gattgccatt    300
attaatcgcc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc tttttaact    360
tcacttgggtt attttattt aaatgartta caaaattttt aatthaagar aatggatgt    420
watattttat tcattaattt ctccctkgt ttacgtwaat tttgaaaaga wtgcattgatt    480
tcttgacaga aatcgatctt gatgtgtgg aagtagttt acccacatcc ctatgagtt    540
ttcttagaat gtataaagggt tgtagcccat cnaacttcaa agaaaaaaaaat gaccacatac    600
tttgcataatca ggctgaaatg tggcatgctn ttctaatcc aactttataa actagcaaann    660
aagtgg                                         665

<210> 197
<211> 492
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(492)
<223> n = A,T,C or G

<400> 197
tttttttttt ttttttttgc aggaaggatt ccatttattt tggatgcatt ttcacaatat      60
atgtttattt gaggcatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg    120

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aaggcagatt cacagaacat gctngtcngc ttgcagttt acctcgtna gatnacagag	180
aattatagtc naaccagtaa acnagaatt tactttcaa aagattaaat ccaaactgaa	240
caaaaattcta ccctgaaaact tactccatcc aaatattgga ataanagtca gcagtgtac	300
attctcttct gaaccttaga tttcttaga aaatatgtaa tagtgatcag gaagagctct	360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc	420
catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatTTT gttcatnctg	480
ancntggctt aa	492
<210> 198	
<211> 478	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(478)	
<223> n = A,T,C or G	
<400> 198	
tttnttttgn attcantct gtannaanta tttcattat gtttattana aaaatatnaa	60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacatgt aacacatacac	120
ttagtatatt ttgaaaagga caagttaaa gtanacncat attgccganc atancacatt	180
tatacatggc ttgattgata ttttagcacag canaaactga gtgagttacc agaaanaaaat	240
natatatgtc aatcngatt aagataaaaa acagatccta tggtacatan catcntgtag	300
gagttgtggc tttatgttta ctgaaagtca atgcagtcc tggtacaaaaga gatggccgta	360
agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtnca	420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa	478
<210> 199	
<211> 482	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(482)	
<223> n = A,T,C or G	
<400> 199	
agtgacttgt ctcaccaacaa aacccttga tcaagttgt ggcactgaca atcagaccta	60
tgctagttcc tgcacatctat tcgctactaa atgcagactg gaggggacca aaaaggggca	120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cgactttga	180
agtgattcag ttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta	240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaaat aaagtcnaga	300
aaatttacct ggangaaaaag aggcttngg ctggggacca tccccattgaa ccttcttta	360
anggacttta agaanaaaact accacatgtn tggtnatcc tggtgccnng ccgtttantg	420
aacntngacn ncaccctnt ggaatanant ctgacngcn tcctgaactt gctcctctgc	480
ga	482
<210> 200	
<211> 270	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(270)	
<223> n = A,T,C or G	

<400> 203

tttttttttt	tttttttga	cccccttctt	ataaaaaaaca	agttaccatt	ttatTTact	60
tacacatatt	tatTTataa	ttggatttag	atattcaaaa	ggcagcttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgctaaagt	180
gaaaatcttc	tctagcttt	ttgactgtaa	atTTTgact	cttgaaaac	atccaaattc	240
atTTTcttg	tctttaaaat	tatctaattct	ttccatTTTt	tccctattcc	aagtcaattt	300
gcttccttag	cctcattttc	tagctttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaca	ggaagagana	atggcacaca	aaacaaacat	tttatattca	tatttctacc	420
tacgttaata	aaatagcatt	ttgtgaagcc	agctcaaaaag	aaggcttaga	tcctttatg	480
tccatTTtag	tcactaaacg	atatcnaaag	tgccagaatg	caaaaggttt	gtgaacattt	540
attcaaaagc	taatataaga	tatTCacat	actcatctt	ctg		583

<210> 204
<211> 589
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(589)
<223> n = A,T,C or G

<400> 204

ttttttttnt	tttttttttt	tttttnctc	ttcttttttt	ttganaatga	ggatcgagtt	60
tttcaactctc	tagatagggc	atgaagaaaa	ctcatcttc	cagcttaaa	ataacaatca	120
aatctcttat	gtatatatcat	atTTtaagtt	aaactaatga	gtcactggct	tatTTctcc	180
tgaaggaaat	ctgttcattc	ttctcattca	tatagttata	tcaagtacta	ccttgcatat	240
tgagaggttt	ttcttctcta	tttacacata	tatTTccatg	tgaatttgta	tcaaaccctt	300
atTTcatgc	aaactagaaaa	ataatgtntt	ctttgcata	agagaagaga	acaatatnag	360
cattacaaaa	ctgctcaaat	tgTTTgttaa	gnTTatccat	tataattagt	tnggcaggag	420
ctaataaaaa	tcacattac	ngacnagcaa	taataaaaact	gaagtaccag	ttaaatatcc	480
aaaataatta	aaggaacatt	tttagcctgg	gtataattag	ctaattcact	ttacaagcat	540
ttattnagaa	tgaattcaca	tgttattatt	ccntagccca	acacaatgg		589

<210> 205
<211> 545
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

<400> 205

ttttnttttt	tttttcaagt	aataatcaga	acaatattta	tttttatatt	taaaattcat	60
agaaaagtgc	cttacattta	ataaaagttt	gtttctaaa	gtgatcagag	gaatttagata	120
tngtctgaa	caccaatatt	aatttgagga	aaatacacca	aaatacatta	agtaaattat	180
ttaagatcat	agagcttgt	agtggaaaaga	taaaatttga	cctcagaaac	tctgagcatt	240
aaaaatccac	tattagcaaa	taaattacta	tgacttctt	gctttaattt	tgtgatgaat	300
atgggtgtc	actggtaaac	caacacattc	tgaaggatac	attacttagt	gatagattct	360
tatgtacttt	gctanatnac	gtggatATGA	gtgacaagt	ttcttcttct	tcaatcttt	420
aaggggcnga	ngaaatgagg	aagaaaagaa	aaggattacg	catactgttc	tttctatngg	480
aaggattaga	tatgtttcct	ttgccaatat	taaaaaata	ataatgtta	ctactagtga	540
aaccc						545

<210> 206
<211> 487

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(487)
 <223> n = A,T,C or G

<400> 206

tttttttttt	tttttagtc	aagtttctna	tttttattat	aattaaagtc	ttggtcattt	60
catttattag	ctctgcaact	tacatattta	aattaaagaa	acgttnntag	acaactgtna	120
caatttataa	atgttaagtg	ccattattga	gtanatatat	tcctccaaga	gtggatgtgt	180
cccttctccc	accaactaat	gaancagcaa	cattagttt	attttattag	tagatnatac	240
actgctgcaa	acgctaattc	tcttctccat	ccccatgtng	atattgtgta	tatgtgtgag	300
tttgttnagaa	tgcatacanca	atctnacaat	caacagcaag	atgaagctag	gcntgggctt	360
tcggtaaaa	tagactgtgt	ctgtctgaat	caaatgatct	gacctatcct	cggtggcaag	420
aactttcga	accgcttcct	caaaggcngc	tgccacattt	gtggcntctn	ttgcacttgt	480
ttcaaaa						487

<210> 207
 <211> 332
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(332)
 <223> n = A,T,C or G

<400> 207

tgaattggct	aaaagactgc	attttanaa	ctagcaactc	ttatttcttt	ccttaaaaaa	60
tacatagcat	taaatcccaa	atcctattta	aagacctgac	agcttgagaa	ggtcactact	120
gcattttag	gaccttctgg	tggttctgct	gttacnnttg	aantctgaca	atcttgana	180
atcttgcat	gcagaggagg	taaaaggtat	tggatttca	cagaggaana	acacagcgca	240
gaaatgaagg	ggccaggcgtt	actgagcttg	tccactggag	ggctcatggg	tgggacatgg	300
aaaagaaggc	agcctaggcc	ctggggagcc	ca			332

<210> 208
 <211> 524
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(524)
 <223> n = A,T,C or G

<400> 208

agggcgtgg	gcggaggggcg	ttactgttt	gtctcagtaa	caataaatac	aaaaagactg	60
gttgtgttcc	ggccccatcc	aaccacgaa	ttgatttctc	ttgtgtcag	agtgactgat	120
tttaaaggac	atggagcttg	tcacaatgtc	acaatgtcac	agtgtgaagg	gcacactcac	180
tcccgctga	tccacattta	gcaaccaaca	atagctcatg	agtccatact	tgttaataact	240
tttgcagaa	tacttntgaa	aacttgcaga	tgataactaa	gatccaagat	atttcccaa	300
gtaaatagaa	gtgggtcata	atattaatta	cctgttcaca	tcagcttcca	tttacaagtc	360
atgagcccag	acactgacat	caaactaagc	ccacttagac	tcctcaccac	cagtcgtcc	420
tgtcatcaga	caggaggctg	tcaccttgac	caaattctca	ccagtcaatc	atctatccaa	480
aaaccattac	ctgatccact	tccggtaatg	caccacccctg	gtga		524

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<210> 209
<211> 159
<212> DNA
<213> Homo sapien

<400> 209
gggtgaggaa atccagagg ttccatggaga aaattccagt gtcagcattc ttgctcctt 60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120
caaaggactc tcgaccctaaa ctgccccaga cccctctcca 159

<210> 210
<211> 256
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(256)
<223> n = A,T,C or G

<400> 210
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgtt 60
actgaatttc tttccacttg gactattaca tgccanttg 120
gggactaatg gaaaaacgta 180
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat
ttgcagggtg naaatgggan ggctggttt 240
ttanatgaac agggacatag gaggtaggca
ccagatgct aaatca 256

<210> 211
<211> 264
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G

<400> 211
acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggagg 60
actgaaacac atacccacat ctttggctg agggataatt ttctgataaa gtcttgctgt 120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga 180
ggggagatac attcngaaag aggactgaaa gaaatactca agtngggaaa cagaaaaaga 240
aaaaaaaggag caaatgagaa gcct 264

<210> 212
<211> 328
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 212
acccaaaaat ccaatgctga atattggct tcattattcc canattctt gattgtcaaa 60
ggatattaatg ttgtctcagc ttgggcacctt cagttaggac ctaaggatgc cagccggcag 120
gttttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccggcag 180

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tttaatttca ttccccatgt a cttgggatcc ttatcatcag ccagagagat tgaaaattta cccctacnac tctttactct ctgganaggg ccagtgggtt tagctataag ctggccaca tttttttttc ctttattcct ttgtcaga	240 300 328
<210> 213	
<211> 250	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(250)	
<223> n = A,T,C or G	
<400> 213	
acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt taaaggatttgc tcactgttgg ggtatagaatgt gactgccagg agggaaagta agccaaggct cattatgcca aagganatatacatttcaat tctccaaact tcttcctcat tccaagagtt ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatac tctctnacct tctcatcggt	60 120 180 240 250
<210> 214	
<211> 444	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(444)	
<223> n = A,T,C or G	
<400> 214	
accggaaatc caatgctgaa tatttggctt cattattccc agattcttg attgtcaaag gattnaatgt tgcactcgact tgggcacttc agttaggacc taaggatgcc agccggcagg tttatatatgt cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt tgaatttcat tcccattgac ttgggatctt tatcatcagc canagagatt gaaaatttac ccctacgact cttaactctc tggagaggc cagtgggtt agctataagc ttggccacat tttttttcc ttatccctt tgcagagat gcatgttcatc catatgctan aaaccaacag agtgactttt acaaaattcc tataganatt gtgaaaaaa ctttacccat agttggcatt acttgcctt ccctaataata cctc	60 120 180 240 300 360 420 444
<210> 215	
<211> 366	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(366)	
<223> n = A,T,C or G	
<400> 215	
acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt taaaggatttgc tcactgttgg ggtatagaatgt gactgccagg agggaaagta agccaaggct cattatgcca aagganatatacatttcaat tctccaaact tcttcctcat tccaagagtt ttcaatattt gcatgaacct gctgataaggc catgttgaga aacaaatatac tctctgaccc tctcatcggt aagcagaggc tggcaac atggaccata gcaaaaaaaa aacttagtaa tccaagctgt tttctacact gtaaccaggc ttccaacca ggtggaaatc tcctataactt	60 120 180 240 300 360

ggtgcc	366
<210> 216	
<211> 260	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(260)	
<223> n = A,T,C or G	
<400> 216	
ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgc	60
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctntnc attttttat	120
taataaaaag tnnaaaaggc ctcttctcaa ctttttccc ttnggctgga aaattnaaaa	180
atcaaaaatt tcctnaagg ntcaagctat catataact ntatcctgaa aaagcaacat	240
aattcttcct tccctccctt	260
<210> 217	
<211> 262	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(262)	
<223> n = A,T,C or G	
<400> 217	
acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgtat	60
tcttgcttat aattttcttat tttataagg aaatagcaaa ttgggggtggg gggaatgttag	120
ggcattctac agttttagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt	180
atgaataatac tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta	240
atatccttca tgcttgtaaa gt	262
<210> 218	
<211> 205	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(205)	
<223> n = A,T,C or G	
<400> 218	
accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca	60
ccccatatcaa ctcccttttg tagtaaactt ggaaccttgg aaatgaccag gccaagactc	120
aggcctcccc agttctactg acctttgtcc ttangtnna ngtccaggg tgcttagaaa	180
anaaaatcagc agacacaggt gtaaa	205
<210> 219	
<211> 114	
<212> DNA	
<213> Homo sapien	
<400> 219	

tactgttttgc tctcagtaac aataaaataca aaaagactgg ttgtgttccg gccccatcca	60
accacgaagt tgatttcctc tgtgtgcaga gtgactgatt taaaaggaca tgga	114
<210> 220	
<211> 93	
<212> DNA	
<213> Homo sapien	
<400> 220	
acttagccagc acaaaaaggca gggtagcctg aattgctttc tgctcttac atttctttta	60
aaataaagcat ttagtgctca gtcctactg agt	93
<210> 221	
<211> 167	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(167)	
<223> n = A,T,C or G	
<400> 221	
actangtgca ggtgcgcaca aatatttgtc gatattccct tcatacttgga ttccatgagg	60
tctttgccc agcctgtggc tctactgttag taagttctg ctgatgagga gccagnatgc	120
cccccaactac cttccctgac gtcffffcana aatcacccaa cctctgt	167
<210> 222	
<211> 351	
<212> DNA	
<213> Homo sapien	
<400> 222	
agggcgttgt gcggaggggcg gtactgacct cattagtagg aggatgcatt ctggcacccc	60
gttcttcacc tgcctcccaa tccttaaaag gccatactgc ataaagtcaa caacagataaa	120
atgtttgtctg aattaaagga tggataaaa aaattaataa tgaatttttgc cataatccaa	180
ttttctcttt tatatttcta gaagaagttt ctttgcgcattt attagatccc gggaatcttt	240
taggtgagca tgatttagaga gcttgcgttg tgctttaca tatatctggc atatttgagt	300
ctcgatcaa aacaatagat tggtaaaggt ggtattatttgc tattgataag t	351
<210> 223	
<211> 383	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(383)	
<223> n = A,T,C or G	
<400> 223	
aaaacaaaca aacaaaaaaaaa acaatttttc attcagaaaa attatcttag ggactgatat	60
tggtaattat ggtcaattta atwrtrttkt gggcatttc cttacattgt cttgacaaga	120
ttaaaatgtc tgcctcccaa ttttgcgttg tattttggaga cttcttatca aaagtaatgc	180
tgccaaagga agtctaagga atttagtagtgc ttcccmmtcac ttgtttggag tgcgttattc	240
taaaagattt tgatttcctg gaatgacaat tatattttaa ctttgggg gaaanagtt	300
ataggaccac agtcttcaact tctgataactt gtaaaatatttgc acttttttg	360
accattaagc tatatgttta aaa	383

<210> 224
 <211> 320
 <212> DNA
 <213> Homo sapien

<400> 224

cccctgaagg ctcttgtta gaaaatagta cagttacaac caataggaac aacaaaaaga
 aaaagttgt gacattgttag tagggagtgt gtaccctta ctccccatca aaaaaaaaaat
 ggatacatgg ttaaaggata raaggggcaat atttatcat atgttctaaa agagaaggaa
 gagaaaaatac tactttctcr aaatggaagc ccttaaaggt gcttgatac tgaaggacac
 aaatgtggcc gtccatcctc cttaragtt gcatgacttg gacacggtaa ctgttgcagt
 ttaractcm gcattgtgac

<210> 225
 <211> 1214
 <212> DNA
 <213> Homo sapien

<400> 225

gaggactgca gcccgcactc gcagccctgg caggcgac tggcatgga aaacgaattg
 ttctgctcg gcgtcctgg gcatccgcag tgggtgtgt cagccgcaca ctgttccag
 aactcctaca ccategggt gggcctgcac agtcttgagg ccgaccaaga gccagggagc
 cagatggtgg aggccagct ctcgtacgg caccagagt acaacagacc ctgctcgct
 aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc
 atcagcattg ctgcgcgtg ccctaccgcg gggacttctt gcctcgttt tggctgggt
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 cagtcccccc ttgtggcacg ttgacccaaac cttaccagtt gtttttcat ttttgtcccc
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<210> 226
 <211> 119
 <212> DNA
 <213> Homo sapien

<400> 226

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<210> 227
 <211> 818
 <212> DNA
 <213> Homo sapien

<400> 227

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acggacggtt cttagcacaa tttgtgaaat ctgtgtaraa ccgggctttg caggggagat	180
aatttcctc ctctggagga aagggtgtga ttgacagcca gggagacagt gacaaggcta	240
gagaaagcca cgctcgccct tctctgaacc aggtggaaac ggcagacccc taaaacgaa	300
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ggaaagggtg caccctcage agagaagccg agagcttaac tctggctgtt tccagagaca	480
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gccatccact ggacatgaag ctgaggacac tgggcttcaa cactgagttg tcatgagagg	600
gacaggctct gcctcaagc cggctgaggg cagcaaccac tctctcccc ttctcacgc	660
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caagaggata tgaggactgt ctcagcctgg ctttggctg acaccatgca cacacacaag	780
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<213> Homo sapien	
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tctggccga cttggctct cttggctgt ttcttaagat gggagtcac attcaatgg	180
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tgctcggtgc acattttgggt gctttggat aaaagattta tgagccaact attctctggc	300
accagattct aggccagttt gttccactga agttttccc acagcagtc acctctgcag	360
gctggcagct gaatggctt cgggtggctc tggcaaga tcacactgag atcgatgggt	420
gagaaggcta ggatgtttgt ctatgtttt tagtgcac gttggctct tccaggttgg	480
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ccgtggatgtt ctttggccca ttccagcagt cccaggatgtt catttcaagt ttgggtttt	600
ttctttctgt taatgttctt ctgtgtgtc agtgccttc atttcttggg ctaagcagca	660
ttgggagatg tggaccagag atccactctt taagaaccag tggcgaaaga cactttctt	720
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<210> 229	
<211> 300	
<212> DNA	
<213> Homo sapien	
<400> 229	
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tgcagggttg ttgttttttta attattattt ttagaaacgt caccacagt ccctgttaat	180
ttgtatgtga cagccactc tgagaaggtc ctatccc acctgcagag gatccagttt	240
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<210> 230	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 230	
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gagcagact tcaaggaggaa gaagcttgca gagcagctca agcaagctga ggagctcagg	120
caatataaaag tcctgggtca cactcaggaa cgagagctga cccagttaa ggagaagttg	180
cggaaaggga gagatgcctc cttctcattt aatgagcatc tccaggccct cttcaactccg	240
gatgaaccgg acaagtccca gggcaggac ctccaagaaa cagacctcgg ccgcgaccac	300
g	301

<210> 231
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 <212> DNA
 <213> Homo sapien

<400> 231
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 caggaactcc aagtccacat ccttggcaac tggggacttg cgccaggtag ccttgaggat 120
 ggcaacacgg gacttctcat caggaagtgg gatgttagatg agctgtatcaa gagggccagg 180
 tctgaggatg gcaggatcaa tgatgtcagg ccgggttggta ccgcataatga tgaacacatt 240
 ttttttgtg gacatgccat ccattctgt caggatctgg ttgatgactc ggtcagcagc 300
 C 301

<210> 232
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 232
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 ggcgacagcg gggcttcctg attctgaaataactttgt gtaaaattaac agccacctat 120
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtctgtcca 180
 cgtgctgtac caagtgtctgg tgccagcctg ttacctgttc tcactaaaaa tctggctaat 240
 gcttttgtt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300
 g 301

<210> 233
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 233
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 cctagaagtt acagagatc tagctggtgc gctggcaccc ctggcctcac acagactccc 180
 gagtagctgg gactacagggc acacagtac tgaagcagggc cctgttagca attctatgcg 240
 tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atccatcaa 300
 C 301

<210> 234
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 234
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 cattttatttc atcatgtatgc ttctttgt ttctttttt cgttttttc tttttttttt 120
 tcaatttcag caacatactt ctcaattttt tcaggattta aaatcttgag ggattgtatct 180
 cgcctcatga cagcaagttc aatgttttg ccacctgact gaaccacttc cagggatgcc 240
 ttgatcacca gcttaatggt cagatcatct gcttcaatgg ctgcgtcagt atagtttttc 300
 t 301

<210> 235
 <211> 283
 <212> DNA
 <213> Homo sapien

<400> 235	
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aattccctca tcttttaggg aatcattac caggtttgg aaggattcg acagctcagg	120
tgcttcact aatgtctctg aacctctgtc cctctttgtt catggatagt ccaataaaata	180
atgttatctt tgaactgtatg ctcataggag agaatataag aactctgagt gatatcaaca	240
ttagggattc aaagaaaat tagatttaag ctcacactgg tca	283
<210> 236	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 236	
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aatacttttta aatcgatcg atttccctaa cccacatgca atcttcttca ccagaagagg	120
tcggagcagc atcatataa ccaagcagaa tgcgtaatag ataaataacaa tggtatata	180
tggtagacg gcttcatgag tacagtgtac tgtgtatcg taatctggac ttgggttgta	240
aagcatcgtg taccagtcg aaagcatcaa tactcgacat gaacgaatat aaagaacacc	300
a	301
<210> 237	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 237	
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actcaattttt tggtcgctcc tttttggcct tttccaattt gtccatctca attttctggg	120
ccttggctaa tgccctcatag taggagtctt cagaccagcc atggggatca aacatatctt	180
ttgggttagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta	240
gggttccgaa attctttctt ctttggata atgtagttca tatccattcc ctcctttatc	300
t	301
<210> 238	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 238	
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gttcacagtt cagccccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca	120
ccttgagact tccggagtcg aggctctcca gggtttccca gcccataat cattttctgc	180
acccctctgc tggaaagcag ctcccgggg ggtggaaatg ggtgactaga agggattca	240
gtgtgggacc caggtctgt tttcacagt aggaggtgga agggatgact aatttctta	300
t	301
<210> 239	
<211> 239	
<212> DNA	
<213> Homo sapien	
<400> 239	
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ttctgtcaaa ccatgataact gagtttgg acaacccaga aataactaag agaaggccaa	120
cataataacct tagagatcaa gaaacattt cacagttca ctgtttaaaa atagctcaac	180
attcagccag tgagtagagt gtgaatgcc gcatacacag tatacagggtc cttcaggga	239
<210> 240	

<211> 300
 <212> DNA
 <213> Homo sapien

<400> 240
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 gctgggttag ccagatgact tctgtccct ggtcactttc ttcaatgggg cgaatgggg 180
 ctgcagggtt ttaaaatca tgcttcatct tgaagcacac ggtcacttca ccctcctcac 240
 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc 300

<210> 241
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 241
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 ctccatcg tattggaaaa ctgcaactg gactcaactg gaagggaaatgt ctgctgccag 180
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtctttct 240
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<210> 242
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 242
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 gtctcaaga atatatcatt ctttttcac tagaaccat tcaaaatata agtcaagaat 180
 cttaatatca acaaataatata caagcaact ggaaggcaga ataactacca taattttagta 240
 taagtaccca aagttttata aatcaaaggc cctaatgata accatttttta gaattcaatc 300
 a

<210> 243
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 243
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 tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcatga tgaccagcgt 180
 gctggtttgt ccagatggca agacagttaga agcagaggct gcccacggga ctgttaaccgg 240
 tcactaccgc atgttccaga aaggacagga gacgtccacc aatcccattt cttccatttt 300
 t

<210> 244
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 244
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 gtcatgcaat cccatggca ggatctgtct gtgcacatgc ctctgttagag agcagcattc 120

ccagggacct tggaaacagt tgacactgta aggtgcttgc tcccaagac acatcctaaa 180
 aggtgttcta atggtaaaaa cgttttcott ctttattgcc ctttcttatt tatgtgaaca 240
 actgtttgtc ttttgttat ctttttaaa ctgtaaagtt caatttgaa aatgaatatac 300

<210> 245
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 245

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 aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccatat 180
 gtttcaaag agcagagatg caattaaata ttgttttagca tcaaaaaggc cactcaatac 240
 agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa 300
 g 301

<210> 246
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 246

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 agtgccttctt gtggaaaattt aataaaacag ttaattcaaa gccttgatatt atgttaccac 180
 taacaatcat actaaatata ttttgaagta caaagtttga catgccttaa agtgacaacc 240
 caaaatgtgtc ttacaaaaca cgttccataac aaggtatgct ttacactacc aatgcagaaa 300
 c 301

<210> 247
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 247

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 ctttgcgtat caaggttggg gcttaagtgg attaaggggag gcaagttctg gttccttgc 240
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 a 301

<210> 248
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 248

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 gtacattcca gcctgttggc aactccataa aaacatttca gatTTTaatc ccgaatttag 240
 ctaatgagac tggatTTTG tttttatgt tttgtgtcgc agagctaaaa actcagttcc 300
 c 301

<210> 249
 <211> 301

<212> DNA
 <213> Homo sapien

<400> 249
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 ccagggagac acagcagtgta ctcagagctg gtcgcacact gtcctccct cccaccggcc 180
 catcgtaatg aattattttg aaaattaatt ccaccatctt ttcagattct ggatggaaag 240
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 a 301

<210> 250
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 250
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 cataaggcaca tcagttactt tctctggctg gaatagtaaa ctaaagatgt gtacatctac 180
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 caataaaacc aaacatgtttt ataaacattaa gaaaaacaat aaagatacat gattgaaacc 300
 a 301

<210> 251
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 251
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 cattggggatc aatgaaaaggc ttcaagaaat cttcaggctc actcttttgc agggccggaa 240
 cctctggagg ggggcagttgg aatcccgatc ccaggacggaa tccctgtcgaa aagatatactt 300
 c 301

<210> 252
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 252
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 atatatcaag caaaactggaa ggcagaataaa ctaccataat ttagtataag tacccaaagt 240
 tttataatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc 300
 a 301

<210> 253
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 253
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<212> DNA	
<213> Homo sapien	
<400> 254	
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<211> 302	
<212> DNA	
<213> Homo sapien	
<400> 255	
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<210> 256	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
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<223> n = A,T,C or G	
<400> 256	
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<210> 257	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 257	
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gtcacattac tcccttcagt gatttcttgt agaagtgcga atccctgaat gccaccaaga	240
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c	301
<210> 258	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 258	
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cccaggccaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg	180
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tggtgatccc tgggagcgtt ggtggagtaa cgttggtcca tggaaagcag cgcccacaac	300
t	301
<210> 259	
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<212> DNA	
<213> Homo sapien	
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<221> misc_feature	
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<400> 259	
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gtgtcctgaa gtgatttggg cccctgaggg cagacaccta agtaggaatc ccagtggaa	120
gcaaagccat aaggaagccc aggattcctt gtgatcagga agtggccag gaaggtctgt	180
tccagctcac atctcatctg catgcacac ggaccggatg cgcccaactgg gtcttggctt	240
ccctccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg	300
c	301
<210> 260	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 260	
ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaaatt aagcaatgg	60
aagggtctt aacttggaaa agatttaggat tcactggttt acaagttata attgaatgaa	120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacaa cagattaac	180
tagggcaaaa taaaataagtg tgtggaaagcc ctgataagtg cttaaaaaac agactgattc	240
actgagacat cagtagctgc ccggggggcc gctcgagccg aattctgcag atatccatca	300
c	301
<210> 261	
<211> 301	
<212> DNA	
<213> Homo sapien	

<400> 261
aaatattcga gcaaatcctg taactaatgt gtctccataa aaggcttga actcagtgaa 60
tctgcttcca tccacgatc tagcaatgac ctctcgaca tcaaagctcc tcttaaggtt 120
agcaccaact attccatatac attcatcagc agggaaaataaa ggcttctcag aaggttcaat 180
ggtgacatcc aatttcttct gataatttag attcctcaca accttccttag ttaagtgaag 240
ggcatgatga tcataccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300
a 301

<210> 262
<211> 301
<212> DNA
<213> Homo sapien

<400> 262
gaggagagcc tgttacagca tttgttaagca cagaatactc caggagtatt tggtaattgtc 60
tggagcttc ttggcgcaag tcttcagaa attaaaaaag atgcaaatcc ctgagtcacc 120
cctagacttc ctaaaccaga tcctctgggg ctggAACCTG gcactctgca tttgttaatga 180
gggctttctg gtgcacacct aattttgtgc atctttgccccc taaatcctgg attagtgc 240
catcattacc cccacattat aatggatag attcagagca gataactctcc agcaaagaat 300
c 301

<210> 263
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 263
tttagcttgt ggttaaatgac tcacaaaaact gatTTaaaaa tcaagttaat gtgaattttg 60
aaaattacta cttaaatccca attcacaata acaatggcat taaggTTGA cttgagttgg 120
ttcttagtat tattttatgtt aaataggctc ttaccacttg caaataactg gcccacatcat 180
taatgactga cttcccagta aggctctca aggggtaagt angaggatcc acaggatttg 240
agatgctaag gccccagaga tcgtttgatc caaccctctt atttcagag gggaaaatgg 300
g 301

<210> 264
<211> 301
<212> DNA
<213> Homo sapien

<400> 264
aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60
aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag 120
gtggatagat ctagaattgtt aacattttaa gaaaaccata scatttgaca gatgagaaaag 180
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240
acccttcata taaattcact atcttggctt gaggcactcc ataaaatgtt tcacgtgcat 300
a 301

<210> 265
<211> 301
<212> DNA
<213> Homo sapien

<400> 265

tgccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt	60
cttcttgcga cgcaattt cttctctggg gagaagccgg gaagtcttct cctggctcta	120
catattcttg gaagtctcta atcaactttt gtccatttg tttcatttct tcaggaggga	180
tttcagttt gtcaacatgt tctctaaaca cacttgccca tttctgtaaa gaatccaaag	240
cagtccaaagg ctttgacatg tcaacaacca gcataactag agtacccctc agagatacgg	300
c	301
<210> 266	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 266	
taccgtctgc ctttcctccc atccaggcca tctgcgaatc tacatggtc ctcttattcg	60
acaccagatc actctttcctt ctaccacag gcttgcatacg agcaagagac acaacctcct	120
ctcttgcgtt ttccagcttc tttctgtt ctcccaccc ctaaggatctt attcttgggg	180
atagagacac caataccat aacctctctc ctaagcctcc ttataacccca gggcacag	240
cacagactcc tgacaactgg taaggccaat gaactggag ctcacagctg gctgtgcctg	300
a	301
<210> 267	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 267	
aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg	60
gttctcagtgttcttccat ccaggaaaag ctcacctaga ctttctgagg ctgaatcttc	120
atcctcacag gcaatctgtt agagcctgtt attccttagcc ttatgtggctt ggatgtaaagc	180
ctcattctgtt ttccctcttca cttttctttt caagttggctt ttccctcacat ccctctgttc	240
aattcgcttc agcttgcgtt ctttagccctt catttccaga agcttcttctt ctttggcattc	300
t	301
<210> 268	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 268	
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt ttctttctta	60
gatcttggga gagctgggttc ttcttaaggag aaggaggaag gacagatgtt accttggatc	120
tcgaagagga agtctaatgg aagtaatttgc tcaacggtcc ttgttttagac tcttggata	180
tgctgggtgg ctcagtgttgc cttttggag aaagcaagttttaa ggatgtaaacca	240
cttccatttgc ttctacttttgc taccatcatc aattgttatattat tatgtattttt ttggagaact	300
a	301
<210> 269	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 269	
taacaatata cactgttat ctttttaact gtccatcatt agcaccaatg aagattcaat	60
aaaattacat ttattcacac atctcaaaac aattctgcaat attcttagtg aagtttact	120
atagtcacag accttaaata ttccatgtt tttctatgtc tactgaaaaat aagtttacta	180
ctttctgttgc tattttttac aaaatcttat taaaatttctt ggtattatca ccccaatta	240
tacagtagca caaccacccat atgtatgttt tacatgtatag ctctgttagaa gttcacatc	300
t	301

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<210> 270
<211> 301
<212> DNA
<213> Homo sapien

<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgc ttaaaaattaa ttaagcctt 60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120
gagttgctg gtgcagtgc tattggataa cactattcat ggccgaaattg atcaagtcaa 180
ccaactcctt gaactggatc atcagaagaa gggtggtgca cgatatactg cactagataa 240
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac 300
a 301

<210> 271
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 271
aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttcattt 60
ttttagctc atctttaggg ttgatattca gttcatgctt cccttgcgt tcttgatcca 120
gaatttcaat cacttcatca gcctgttattc gctccaaattc tctataaagt gggtccaagg 180
tgaaccacag agccacagca caccttttc ctttggtgac tgccttcacc ccatganggt 240
tcttcctcc agatganaac tgatcatgctt cccacattt gggtttata gaagcagtca 300
c 301

<210> 272
<211> 301
<212> DNA
<213> Homo sapien

<400> 272
taaattgcta agccacagat aacaccaatc aatggaca aatcaactg tc ttcaaattgtc 60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtattttagga 120
tccaaataatt ccctcatgtat gagcaagaaa aattctttgc gcacccctcc tgcatccaca 180
gcatcttc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttggtttc 240
ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaaggcag 300
g 301

<210> 273
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 273
acatgtgtgt atgtgtatct ttggggaaaan aanaagacat cttgttayt attttttgg 60
agagangctg ggacatggat aatcacwttaa tttgctayta tyactttaat ctgactyga 120

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gaaccgtctta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatccacc	180
ttytttctgt ccagagagag tatcatgac ananatttma gggtaamac atgmattgg	240
gggacttny tttacngagm accctgcccsg sgccctcg makcngantt ccgcsananc	300
t	301
<210> 274	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 274	
cttatatact ctttctcaga ggcaaaagag gagatggta atgttagacaa ttctttgagg	60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaaatt aacttgtaaa	120
tgattctctt tgaaatctga atgagatcaa gaggccagct ttagctgtg gaaaagtcca	180
tctaggtatg gttgcattct cgtctcttt tctgcagtag ataatgaggt aaccgaaggc	240
aatttgtctt ctttgataa gaagcttct tggcatatc agggaaattcc aganaaaatgc	300
c	301
<210> 275	
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
<400> 275	
tcgggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg	60
gggtgaaatt gccaacctt ctattaactt atgttggcaa tttgcacc aacagttaagc	120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacgaaatata agtagtggag	180
tcaagagact cccaggcctc agcgtacctg cccggggggc cgctcgaagc cgaattctgc	240
agatatatccat cacactggcg gnccgtcgan catgcatactaa gaaggnccaa ttgccctat	300
a	301
<210> 276	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 276	
tgtacacata ctcataataat aaatgactgc attgtggtat tattactata ctgattat	60
ttatcatgtg acttctaatt agaaaatgtt tccaaaagca aaacagcaga tataaaaaat	120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc	180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt	240
aaaactattc agtatgtttc cttgttca tgtctgagaa ggctctcattt caatggggat	300
g	301
<210> 277	
<211> 301	
<212> DNA	
<213> Homo sapien	

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<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 277
tttgttcatg tcagtatttt attacttgcg ttatgagtgc tcacccggaa aattctaaag      60
atacagagga cttggagaa gcagagcaac tgaatttaat taaaagaag gaaaacattg      120
gaatcatggc actcctgata ctccccaaa tcaacactct caatccccca ccctcgct      180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga      240
gttcnctgtc gattacatct gaccagtctc cttttccga agtccntccg ttcaatcttg      300
c                                         301

<210> 278
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 278
taccactaca ctccaggcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat      60
aacatatcaa atgaaacacgg gaaaatgaag ctgacaattt atgaaagcca gggcttgc      120
cagtcctcac tggttattatg cattacctgg gaattttat aagcccttaa taataatgc      180
aatgaacatc tcatgtgtc tcacaatgtt ctggcaactat tataagtgtc tcacagggtt      240
tatgtgttct tcgtaacttt atggantagg tactcgcccg cgaacacgct aagccgaatt      300
c                                         301

<210> 279
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 279
aaagcagggaa tgacaaagct tgctttctg gtagttcta ggtgtattgt gactttact      60
gttattttaa ttgcataat aagtaaatat agattatata tgtatagtgt ttcacaaagc      120
tttagacctt accttccagc caccccacag tgcttgatat ttcaagatca gtcattggtt      180
atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcaactac      240
catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag      300
a                                         301

<210> 280
<211> 301
<212> DNA
<213> Homo sapien

<400> 280
ggtaactggag tttccccc ctgtaaaaac gtaactactg ttgggagtg attgaggatg      60
tagaaaggtg gtggAACCA attgtgtca atggaaatag gagaatatgg ttctactct      120

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tgagaaaaaa acctaaggatt agcccaggta gttgcctgta acttcagttt ttctgcctgg	180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcg gacaaagaga	240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag	300
t	301
<210> 281	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 281	
aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc	60
gccgagcaat ccaaattctg aatgaagggg catcttctga aaaaggagat ctgaatctca	120
atgtgttagc aatggcttta tcgggttata cgatgagaa gaactccctt tggagagaaa	180
tgttagcac actgcgatta cagctaaata acccgatattt gtgtgtcatg tttcatttc	240
tgacaagtga aacaggatct tacgatggag tttgtatga aaacaagtt gcagtacctc	300
g	301
<210> 282	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 282	
caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca	60
tccagaaccc aaaaattaag aaattaaaa agacattttt tggtcacctg ctagcacaga	120
agcgcagaag caaagccccag gcagaaccat gctaaccctt cagctcagcc tgcacagaag	180
cgcagaagca aagccccaggc agaaccatgc taaccttaca gctcaggctg cacagaagcg	240
cagaacaaa gcccaggcag aacatgctaa ccttacagct cagcctgcac agaaggcacag	300
a	301
<210> 283	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 283	
atctgtatac ggcagacaaa ctttatarag ttagagagg tgagcggaaag gatgcaaaag	60
cacttgagg gctttataat aatatgctgc ttggaaaaaa aaatgtgttag ttgtatactca	120
gtgcatactcc agacatagta aggggttgc ctgaccaatc aggtgtatcat tttttctatc	180
acttcccagg ttttatgcaa aaattttgtt aaattctata atgggtatat gcatcttttta	240
ggaacacatat acatttttaa aaatctatTT tatgtaaagaa ctgacagacg aatttgcTTT	300
g	301
<210> 284	
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 284	
caggtacaaa acgctattaa gtggcttaga atttgaacat ttgtggctt tattttacttt	60
gcttcgtgtg tggcaaaagc aacatcttcc ctaaatatattt attaccaaga aaagcaagaa	120
gcagattagg tttttgacaa aacaaacagg cccaaagggg gctgacccgg agcagagcat	180
ggtgagaggc aaggcatgag agggcaagtt ttttgtggac agatctgtgc ctactttatt	240
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt	300
a	301
<210> 285	


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<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 289
ggtagactgt ttccatgtta tgtttctaca cattgctacc tcagtgtcc tggaaactta      60
gctttgatg tctccaagta gtccacccctc atttaactct ttgaaaactgt atcatcttg      120
ccaagtaaga gtgggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa      180
cgttctataa atgaatgtgc tgaagcaaag tggccatggt ggcggcgaan aagagaaaga      240
tgtgtttgt tttggactct ctgtggtccc ttccaatgct gtgggttcc aaccagngga      300
a                                         301

<210> 290
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 290
acactgagct ttcttgata aatatacaga atgcttggca tataacaagat tctatactac      60
tgactgatct gttcatttct ctcacagctc ttaccccaa aagctttcc accctaagtg      120
ttctgacctc cttttctaat cacagtaggg atagaggcag anccacctac aatgaacatg      180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc      240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagttag      300
a                                         301

<210> 291
<211> 301
<212> DNA
<213> Homo sapien

<400> 291
caggtaccaa tttcttctat cctagaaaaca ttccatTTTA tgTTGTTGAA acataacaac      60
tatatacgct agatTTTTTT TCTATGCTT acctgctatg gaaaatttga cacattctgc      120
tttactcttt tgTTTatAGG tgaatcacaa aatgtatTTT tatgtattct gtatTTcaat      180
agccatggct gtttacttca tttaatttt ttagcataaa gacattatga aaaggcctaa      240
acatgagctt cacttccccca ctaactaattt agcatctgtt atttcttaac cgtaatgcct      300
a                                         301

<210> 292
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 292

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accttttagt agtaatgtct aataataaat aagaaaatcaa ttttataagg tccatatagc 60
 tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gtgggtattc 120
 aaaaccaaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg 180
 gaaaatatacg tasttyatga atgttnatta aattccaggta ataatagtgg ctacacactc 240
 tcactacaca cacagacccc acagtcctat atgccacaaa cacattcca taacttgaaa 300
 a 301

<210> 293
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 293

ggtaccaagt gctgggtgcca gcctgttacc ttttctcaact gaaaagtctg gctaattgctc 60
 ttgtgttagtc acttctgatt ctgacaatca atcaatcaat ggccttagagc actgactgtt 120
 aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaca gctgttctgt 180
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcattttaa tgacacctgg 240
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggccggcc gctcgagcat 300
 g 301

<210> 294
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 294

tgaccctataa caatatacac tagcttatctt tttaactgtc catcattagc accaatgaag 60
 attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaattt cttagtgaag 120
 tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag 180
 ttcactactt ttctgggata ttctttacaa aatcttattaa aattctctgg tattatcacc 240
 cccaattata cagtagcaca accaccctt gtattttta catgataagct ctgttagaggt 300
 t 301

<210> 295
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 295

gtactcttcc tctccctcc tctgaattta attcttcaa cttgcaattt gcaaggatta 60
 cacatttcac tgtgtatgtat attgtgttgc aaaaaaaaaa gtgtcttgc ttaaaattac 120
 ttgggttgat aatccatctt gcttttccc cattgaaact agtcattaaac ccattctgt 180
 actggtagaa aaacrtctga agagctgtc tatcagcatc tgacaggtga attggatgg 240
 ttcagaacc atttcaccca gacagcctgt ttctatctg tttaataaat tagttgggt 300
 tctct 305

<210> 296
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 296

aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgtatct 60

cacctagtag taaaactaaaa ataaactgaa actttatgga atctgaagtt atttcccttg attaaataga attaataaac caaatatgagg aaacatgaaa ccatgcatac tactatcaac tttggaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtatt tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg c	120 180 240 300 301
 <210> 297	
<211> 300	
<212> DNA	
<213> Homo sapien	
 <220>	
<221> misc_feature	
<222> (1)...(300)	
<223> n = A,T,C or G	
 <400> 297	
actgagttt aactggacgc caagcaggca aggctggaag gttttgtct ctgggtgcta aagggtttaa aacaccttggaa ggagaatcat ttggacaaga agtacttaag agtctagaga acaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttggcctgt tccatcatttggagtgcaact ggccatccct caaaatttggt ctgggtgtgc ctgagtgggt accgcacccgc ggcgcgacc acgtaagcc gaattctgca gatatccatc acactgggg t	60 120 180 240 300
 <210> 298	
<211> 301	
<212> DNA	
<213> Homo sapien	
 <220>	
<221> misc_feature	
<222> (1)...(301)	
<223> n = A,T,C or G	
 <400> 298	
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 <210> 299	
<211> 301	
<212> DNA	
<213> Homo sapien	
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gctgcattcc acaagggtct cagctaatac agtttcaacta cctgcagtc tcaaaaactta 180
gtaaaagcaag accatgacat tccccacgg aaatcagagt ttgcccacc gtcttggta 240
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g 301

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<400> 301
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ggaaactcac aaagaccctc agagctgaga cacccacaac agtgggagct cacaagacc 180
ctcagagctg agacacccac aacagtggga gtcacaaag accctcagag ctgagacacc 240
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t 301

<210> 302
<211> 301
<212> DNA
<213> Homo sapien

<400> 302
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g 301

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<213> Homo sapien

<400> 303
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tggctaatgg aactaccgct tgcattaa aatgggttgt ttgtgaaatg atcataggcc 180
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c 301

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<212> DNA
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<400> 304
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cttttttagtg tatcatatca ggaatcatct cacattgggt ttgtgcattt ctgggtcagt 180
gactttcagc cacttgggtt aggtggagtt ggccatatgt ctccactgca aaattactga 240

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<212> DNA	
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<223> n = A,T,C or G	
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cagggggaca gacctggaca gacacgttgc catttgcgc tgtggtagg aaaaatggcg	120
taaaggagga gaaacagata caaaatctcc aactcagttt taaggatttc tcattgcctag	180
aatatttggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaaacaaaa	240
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attggaaata gatacttgag cccaaagagc attcaatcat tgttttatgccttmtttt	180
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cacatagcac cggagatatg agatcaacag ttcttagcc atagagattc acagcccaga	300
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<211> 647	
<212> DNA	
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<221> misc_feature	
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ccaccctct gacccttgg aactcctctg accctttaga acaagcctac ctaatatctg 240
ctagagaaaa gaccaacaac ggcctcaaag gatctttac catgaaggc tcagctaatt 300
cttggcttaag atgtgggttc cacattaggt tctgaatatg ggggaaaggc tcaatttgct 360
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<210> 309
<211> 460
<212> DNA
<213> Homo sapien

<400> 309
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<210> 310
<211> 539
<212> DNA
<213> Homo sapien

<400> 310
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atgattatgt cattacatgt atggtagtga tggggatgat aggaagaaag aacttatggc 480
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<210> 311
<211> 526
<212> DNA
<213> Homo sapien

<220>
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attaaacatg gaataaaagat ttgtccttaa atataatcta caagaagact ttgatatttg	240
ttttcacaa gtgaaggcatt cttataaaagt gtcataacct ttttgggaa actatggaa	300
aaaatggga aactctgaag ggtttaagt atcttacctg aagctacaga ctccataacc	360
tctcttaca gggagctct gcagccccta cagaaatgag tggctgagat tcttgattgc	420
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<223> n = A,T,C or G	
<400> 312	
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tgctaatgtg gtttctttg taaaccanga tt当地tatttg nctggatatacgat aatatcagct	420
ctgaacgtgt gtaaagattt tttgttgg aatataggag aaatcagttt gctgaaaaagt	480
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<210> 313	
<211> 718	
<212> DNA	
<213> Homo sapien	
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<222> (1)...(718)	
<223> n = A,T,C or G	
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<223> n = A,T,C or G

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cacacaatg caatagttgg tcactgcatt tttacctgaa ccaaagctaa acccggtgtt   360
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<210> 325
<211> 400
<212> DNA
<213> Homo sapien

<400> 325
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<210> 326
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<212> DNA
<213> Homo sapien

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<210> 327
<211> 220

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<212> PRT
<213> *Homo sapien*

<400> 327
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 35 40 45
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
 50 55 60
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
 65 70 75 80
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
 85 90 95
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
 100 105 110
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
 115 120 125
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
 130 135 140
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
 145 150 155 160
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
 165 170 175
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
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 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
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 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 210 215 220

<210> 328
<211> 234
<212> DNA
<213> *Homo sapien*

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<210> 329
<211> 77
<212> PRT
<213> *Homo sapien*

<400> 329
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 35 40 45
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
 50 55 60

Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
 65 70 75

<210> 330
 <211> 70
 <212> DNA
 <213> Homo sapien

<400> 330
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<210> 331
 <211> 22
 <212> PRT
 <213> Homo sapien

<400> 331
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 Val Ser Gly Ser Cys Ser 20

<210> 332
 <211> 2507
 <212> DNA
 <213> Homo sapien

<400> 332
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<210> 333

<211> 3030

<212> DNA

<213> Homo sapien

<400> 333

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tgggagcggg agggggggcggy aatctgtcg cccactcccc tctgaccagc caccggcg	240
cgcctacgct gatgectgt gtcaactatg ccccttggaa tctgcccggc tcggcggagc	300
cgccaaagca atgccaccca tggccctgggg tggcccgagg gacgtccccca gctccgtgc	360
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gacatgactc cctgttgcct gtggacagtt accagtcttgc ggcctctcgct ggtggctgg	660
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aacgcattcc gtacagcaag gggcagttgc gggagctggaa gcggggatgt ggcgctaaca	840
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<210> 334

<211> 2417

<212> DNA

<213> Homo sapien

<400> 334

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gaatgtgc	cattgaggat	atctaaactt	agatcaattt	cattttccct	ccaaagactat	300
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tatgccat	atatgtaaaa	gcaacatcata	agctctctaa	tcatgctcac	ctaaaagatt	420
cccggtatct	aataggctca	aagaaacttc	ttcttagaaat	ataaaagaga	aaattggatt	480
atgc	aaaat	tcattattaa	ttttttcat	ccatccttta	attcagcaaa	540
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acagcctg	ctgccc	aggctg	gatccccat	ccgggtcaac	cgtatcaa	2220
atcagg	ccggag	ctgg	ccagccctgg	ggtgagttgg	ctcctgtgt	2280

ggtaactgaga caatattgtc ataaaattcaa tgcgccttgc tatccctttt tcttttttat	2340
ctgtctacat ctataatcac tatgcatact agtctttgtt agtgtttcta ttcmacttaa	2400
tagagatatg ttatact	2417

<210> 335
<211> 2984
<212> DNA
<213> *Homo sapien*

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 aaagtaccca tgttttatt agaaaaaaaaaaaaaaa aaaaaaaaaaaa aaaa 2984

<210> 336
 <211> 147
 <212> PRT
 <213> Homo sapien

<400> 336
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 Leu Asp Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr
 20 25 30
 Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
 35 40 45
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
 50 55 60
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
 65 70 75 80
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
 85 90 95
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
 100 105 110
 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
 115 120 125
 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
 130 135 140
 Ala Phe Trp
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<210> 337
 <211> 9
 <212> PRT
 <213> Homo sapien

<400> 337
 Ala Leu Thr Gly Phe Thr Phe Ser Ala
 1 5

<210> 338
 <211> 9
 <212> PRT
 <213> Homo sapien

<400> 338
 Leu Leu Ala Asn Asp Leu Met Leu Ile
 1 5

<210> 339
 <211> 318
 <212> PRT
 <213> Homo sapien

<400> 339
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 1 5 10 15
 Leu Tyr Met Ala Ala Pro Gln Ile Arg Lys Met Leu Ser Ser Gly Val

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35	40	45
Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg		
50	55	60
Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu		
65	70	75
Val Ala Lys Glu Ile Gln Thr Thr Gly Asn Gln Gln Val Leu Val		
85	90	95
Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys		
100	105	110
Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala		
115	120	125
Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met		
130	135	140
His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu		
145	150	155
Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser		
165	170	175
Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly		
180	185	190
Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala		
195	200	205
Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly		
210	215	220
Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val		
225	230	235
Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe		
245	250	255
Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu		
260	265	270
Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His		
275	280	285
Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg		
290	295	300
Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp		
305	310	315

<210> 340

<211> 483

<212> DNA

<213> Homo sapien

<400> 340

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ctccctgctgc aggctggagt gtcttattc ctggcgggag accgcacatt ccactgctga	180
ggtttgtgggg gcggtttatac aggcagtgtat aaacataaga tgtcatattcc ttgactccgg	240
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gctccaaacg tgacatcaact gatgtcttc tcgggggtgc tcatggcccg ctgggtcacg	360
tgctcaatct cgccattcga ctcttgcctt aactgtatg aagacacctg actgcacgtt	420
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ctg	483

<210> 341

<211> 344

<212> DNA

<213> Homo sapien

<400> 341
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 gtcgccttac aagtattaaa tattttactt cttccataa agatgtctc aaaatatgca 180
 attaatttaa taatttctga tgatggttt atctgcagta atatgtatat catctattag 240
 aatttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc 300
 ctgattctta acattgtctt taatgaccac aagacaacca acag 344

<210> 342
 <211> 592
 <212> DNA
 <213> Homo sapien

<400> 342
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 caatgtggaa acttcttata cttgggttcca ttatgaagtt ggacaattgc tgctatcaca 120
 cctggcaggt aaaccaatgc caagagatg atggaaacca ttggcaagac ttttgtatg 180
 accaggattt gatattttata aaaatattgt tgatggaaag ttgctaaagg gtgaattact 240
 tccctcagaa gagtgtaaag aaaagtctaga gatgtctataa tagcagctat tttaattggc 300
 aagtgccact gtggaaagag ttccctgtgt tgctgaagtt ctgaaggcgt gtcaaattca 360
 tcagcatggg ctgtttgtgt caaatgcaaa agcacaggc tttttagcat gctggctct 420
 cccgtgtcct tatgcaataa atcgctttct tctaaatttc tcctagctt catttccaa 480
 agttttctt ggtttgtat gtctttctg ctttccatta attctataaa atagtatggc 540
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<210> 343
 <211> 382
 <212> DNA
 <213> Homo sapien

<400> 343
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 cttgttaactc tcccttctcc ttcttcccc tttctctgccc cgccttccc atctgctgt 180
 agacttcttg attgtcagtc tggcatacat ccagtgattt tttgggttgc tggcccttt 240
 ctgactgccc aaggggctca gaaccccagec aatcccttcc tttcactacc ttctttttg 300
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 aaaccaccaa gctgaaaaaaaaaa aa 382

<210> 344
 <211> 536
 <212> DNA
 <213> Homo sapien

<400> 344
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 gtttaggggg atgccaaggaa taaggccagc tcagttatataa gaagagaagc agaacaacaaa 180
 agtctttcag agaaatggat gcaatcagag tggatcccg gtcacatcaa ggtcacactc 240
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 tcgaccctat atccccccgc cgcgtccctt tctccataaa attcttcttta gtagcttataa 360
 ctttcttatt atttgatcta gaaatttgc tcttttacc cctaccatga gccctacaaa 420
 caactaacct gccactaata gttatgtcat ccctcttatt aatcatcatc ctggccctaa 480
 gtctggccta tgagtacta caaaaaggat tagactgagc cgaataacaa aaaaaaa 536

<210> 345
 <211> 251

<212> DNA
 <213> Homo sapien

<400> 345
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 gcgtggcca gaaatcaca tcctacactg cccaggagcc agacacattt atgaacaga 180
 aaataacata tcggatttg agagacactg ccaactggct ggagattaat ccggacactg 240
 gtgcatttc c 251

<210> 346
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G

<400> 346
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 ctaagtcttg ttacaaaaaa aaggaaaaag aaaagatctt ctcagttaca aattctggga 120
 agggagacta tacctggctc ttgccttaag tgagaggctc tccctcccgc accaaaaaat 180
 agaaaggctt tctatttcac tggccaggt aggggaagg agagtaactt tgagtctgtg 240
 ggtctcattt cccaaagggtgc cttcaatgct catnaaaaacc aa 282

<210> 347
 <211> 201
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(201)
 <223> n = A,T,C or G

<400> 347
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 tctgagactg actggaccca cccagaccca gggcaaagat acatgttacc atatcatctt 180
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<210> 348
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 348
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 aggagacact cccagcatgg aggagggtt atctttcat cctaggtcag gtctacaatg 180
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 gcccgcctc c 251

<210> 349
 <211> 251
 <212> DNA

<213> Homo sapien

<400> 349

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cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt	180
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<210> 350

<211> 908

<212> DNA

<213> Homo sapien

<400> 350

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<210> 351

<211> 472

<212> DNA

<213> Homo sapien

<400> 351

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<210> 352

<211> 251

<212> DNA

<213> Homo sapien

<400> 352

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caggctgcgt tccgtcctta cgatgaagac cacgatgcag tttccaaaca ttgcactac	180
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<212> DNA
<213> Homo sapien

<400> 353
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gataaggcaa cttatacatt gacaatccaa atccaataca tttaaacatt tggaaatga 240
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gggctcctaa tgttagt 436

<210> 354
<211> 854
<212> DNA
<213> Homo sapien

<400> 354
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acacgggatg tcag 854

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<211> 676
<212> DNA
<213> Homo sapien

<400> 355
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gacagcatcg ctgtaaaaag cctaccaatg agagctcagt tcaaggcgaa ccaccccttc 240
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<210> 356

<211> 574
 <212> DNA
 <213> Homo sapien

<400> 356
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 agctttgcag ctttgcga acagtacttt ccca 574

<210> 357
 <211> 393
 <212> DNA
 <213> Homo sapien

<400> 357
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 aagccacaac caaracttga ttttatcaac aaaaacccct aaatataaac ggsaaaaaaag 180
 atagatataaa ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara 240
 araaraataag ttttatatgg aaagaaggc attcaagcac actaaaraaa cctgaggkaa 300
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<210> 358
 <211> 630
 <212> DNA
 <213> Homo sapien

<400> 358
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<210> 359
 <211> 620
 <212> DNA
 <213> Homo sapien

<400> 359
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<213> Homo sapien	
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<400> 363

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<210> 364

<211> 401

<212> DNA

<213> Homo sapien

<400> 364

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<210> 365

<211> 356

<212> DNA

<213> Homo sapien

<400> 365

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<210> 366

<211> 1851

<212> DNA

<213> Homo sapien

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<210> 367

<211> 668

<212> DNA

<213> Homo sapien

<400> 367

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<210> 368

<211> 1512

<212> DNA

<213> Homo sapien

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agaagcatta gagggtacag tttttttttt ttaaatgcac ttctggtaaa tactttttt	1260
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<210> 369
<211> 1853
<212> DNA
<213> Homo sapien

<400> 369

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ttcaaaacaga ttggaaacccc ggaggtaacct gctagttgtt gaaactgggtt ggttagacgcg	180
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tccatgccgg ctgtttttt tttttttttt tttttttttt tttttttttt tttttttttt	300
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<210> 370
<211> 2184
<212> DNA

<213> Homo sapien

<400> 370

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ggagttcttc	tttcatagtt	catccatatg	gctccagagg	aaaattatat	tatttttta	480
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<210> 371

<211> 1855

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1855)

<223> n = A,T,C or G

<400> 371

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<210> 372

<211> 1059

<212> DNA

<213> Homo sapien

<400> 372

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<210> 373

<211> 1155

<212> DNA

<213> Homo sapien

<400> 373

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<210> 374
<211> 2000
<212> DNA
<213> *Homo sapien*

<400> 374	
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tgtt agaaaagaaaa agacatcttgc catggaaaata gtacgttgcg ggaagaaaatt	1920

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<210> 375
 <211> 2040
 <212> DNA
 <213> Homo sapien

<400> 375

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aaacagatgc	caaataactc	ttctgaaaac	agcaacccag	aacaagactt	aaagctgaca	1500
tcagaggaag	agtcacaaaag	gtttgagggc	agtgaaaatg	gccagccaga	gaaaagatct	1560
caagaaccag	aaataaataa	ggatgggtat	agagagctag	aaaattttat	ggctatcgaa	1620
gaaatgaaga	agcacggaa	tactcatgtc	ggattccccag	aaaacctgac	taatggtgc	1680
actgctggca	atggtgatga	tggattaatt	cctccaagga	agagcagaac	acctgaaagc	1740
cagcaatttc	ctgacactga	gaatgaagag	tatcacagt	acgaacaaaa	tgatactcg	1800
aagcaatttt	gtgaagaaca	gaacactgga	atattacacg	atgagattct	gattcatgaa	1860
gaaaagcaga	tagaagtgg	tgaaaaaaatg	aattctgagc	tttctcttag	ttgtaaagaaa	1920
gaaaagagaca	tcttgcatga	aaatagtacg	ttgcgggaag	aaattgcct	gctaagactg	1980
gagctagaca	caatgaaaca	tcagagccag	ctaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	2040

<210> 376
 <211> 329
 <212> PRT
 <213> Homo sapien

<400> 376

Met	Asp	Ile	Val	Val	Ser	Gly	Ser	His	Pro	Leu	Trp	Val	Asp	Ser	Phe
1				5				10				15			
Leu	His	Leu	Ala	Gly	Ser	Asp	Leu	Leu	Ser	Arg	Ser	Leu	Met	Ala	Glu
				20				25				30			
Glu	Tyr	Thr	Ile	Val	His	Ala	Ser	Phe	Ile	Ser	Cys	Ile	Ser	Ser	Ser
				35				40			45				
Leu	Asp	Gly	Gln	Gly	Glu	Arg	Gln	Glu	Gln	Arg	Gly	His	Phe	Trp	Arg
				50				55			60				

Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
 65 70 75 80
 Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
 85 90 95
 Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
 100 105 110
 His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
 115 120 125
 Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
 130 135 140
 Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
 145 150 155 160
 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
 165 170 175
 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
 180 185 190
 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
 195 200 205
 Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
 210 215 220
 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
 225 230 235 240
 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
 245 250 255
 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
 260 265 270
 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
 275 280 285
 Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
 290 295 300
 Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
 305 310 315 320
 Ser Met Leu Phe Leu Val Ile Ile Met
 325

<210> 377
 <211> 148
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(148)
 <223> Xaa = Any Amino Acid

<400> 377
 Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
 1 5 10 15
 Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
 20 25 30
 Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
 35 40 45
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
 50 55 60
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
 65 70 75 80
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
 85 90 95

Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
 100 105 110
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
 115 120 125
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
 130 135 140
 Lys Asn Lys Val
 145

<210> 378
 <211> 1719
 <212> PRT
 <213> Homo sapien

<400> 378

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val

	340	345	350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met	Leu Lys Ile		
355	360	365	
Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr	Arg Asn Lys		
370	375	380	
Pro Arg Thr His Met Val Val Glu Val Asp Ser Met Pro	Ala Ala Ser		
385	390	395	400
Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met Gly	Lys Trp Cys		
405	410	415	
Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser	Asn Val Gly		
420	425	430	
Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr	Leu Arg Ser Lys		
435	440	445	
Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys Arg	Gly Ser Gly		
450	455	460	
Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser	Ala Met Lys		
465	470	475	480
Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys	Phe Pro Cys		
485	490	495	
Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp Gly	Asp Tyr Asp		
500	505	510	
Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg Gly	Glu Asp Leu		
515	520	525	
Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro	Arg Lys Asp		
530	535	540	
Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys	Asp Lys Gln		
545	550	555	560
Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly	Asn Ser Glu Val		
565	570	575	
Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn Val	Leu Asp Asn		
580	585	590	
Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln	Glu Asp Glu		
595	600	605	
Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro	Asn Ile Pro Asp		
610	615	620	
Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr	Asn Glu Asp Lys		
625	630	635	640
Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile	Glu Ser Lys		
645	650	655	
Asn Lys His Gly Leu Thr Pro Leu Leu Gly Val His	Glu Gln Lys		
660	665	670	
Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala	Asn Leu Asn Ala		
675	680	685	
Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala	Val Cys Cys Gly		
690	695	700	
Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn	Ile Asp Val Ser		
705	710	715	720
Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr	Ala Val Ser Ser		
725	730	735	
His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr	Lys Glu Lys Gln		
740	745	750	
Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu	Gln Asp Leu Lys		
755	760	765	
Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly	Ser Glu Asn Ser		
770	775	780	
Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn	Lys Asp Gly Asp		
785	790	795	800
Arg Glu Val Glu Glu Met Lys Lys His Glu Ser Asn	Asn Val Gly		

805	810	815
Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn		
820	825	830
Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe		
835	840	845
Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser		
850	855	860
Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn		
865	870	875
Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu		880
885	890	895
Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile		
900	905	910
Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn		
915	920	925
Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro		
930	935	940
Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu		
945	950	955
Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe		960
965	970	975
Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His		
980	985	990
Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser		
995	1000	1005
Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu		
1010	1015	1020
Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His		
1025	1030	1035
Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met		1040
1045	1050	1055
Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met		
1060	1065	1070
Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys		
1075	1080	1085
Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr		
1090	1095	1100
Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys		
1105	1110	1115
Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp		1120
1125	1130	1135
Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His		
1140	1145	1150
Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp		
1155	1160	1165
Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg		
1170	1175	1180
Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val		
1185	1190	1195
Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys		1200
1205	1210	1215
Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly		
1220	1225	1230
Asn Ser Glu Val Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn		
1235	1240	1245
Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys		
1250	1255	1260
Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro		

1265	1270	1275	1280
Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr			
1285	1290	1295	
Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp			
1300	1305	1310	
Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val			
1315	1320	1325	
His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala			
1330	1335	1340	
Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala			
1345	1350	1355	1360
Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn			
1365	1370	1375	
Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr			
1380	1385	1390	
Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr			
1395	1400	1405	
Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu			
1410	1415	1420	
Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly			
1425	1430	1435	1440
Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn			
1445	1450	1455	
Lys Asp Gly Asp Arg Glu Val Glu Glu Met Lys Lys His Glu Ser			
1460	1465	1470	
Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly			
1475	1480	1485	
Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu			
1490	1495	1500	
Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys			
1505	1510	1515	1520
Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser			
1525	1530	1535	
Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu			
1540	1545	1550	
Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser			
1555	1560	1565	
Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe			
1570	1575	1580	
Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe			
1585	1590	1595	1600
Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly			
1605	1610	1615	
Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro			
1620	1625	1630	
Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln			
1635	1640	1645	
Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile			
1650	1655	1660	
Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser			
1665	1670	1675	1680
Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn			
1685	1690	1695	
Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr			
1700	1705	1710	
Met Lys His Gln Ser Gln Leu			
1715			

<210> 379
 <211> 656
 <212> PRT
 <213> Homo sapien

<400> 379
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
 385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415

Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
 450 455 460
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
 465 470 475 480
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
 500 505 510
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
 515 520 525
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
 530 535 540
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
 545 550 555 560
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
 565 570 575
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
 580 585 590
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
 595 600 605
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
 610 615 620
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
 625 630 635 640
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 645 650 655

<210> 380
 <211> 671
 <212> PRT
 <213> Homo sapien

<400> 380
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala

Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
165							170						175		
180							185						190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
195							200						205		
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
210							215						220		
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225							230						235		
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
245							250						255		
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
260							265						270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
275							280						285		
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
290							295						300		
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305							310						315		
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
325							330						335		
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
340							345						350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
355							360						365		
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
370							375						380		
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385							390						395		
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
405							410						415		
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
420							425						430		
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
435							440						445		
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
450							455						460		
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465							470						475		
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
485							490						495		
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu	
500							505						510		
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp
515							520						525		
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys
530							535						540		
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala
545							550						555		
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg
565							570						575		
Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His
580							585						590		
Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln	Lys	Gln	Phe	Cys	Glu	Glu	Gln	Asn
595							600						605		
Thr	Gly	Ile	Leu	His	Asp	Glu	Ile	Leu	Ile	His	Glu	Glu	Lys	Gln	Ile
610							615						620		
Glu	Val	Val	Glu	Lys	Met	Asn	Ser	Glu	Leu	Ser	Leu	Ser	Cys	Lys	Lys

625	630	635	640
Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala			
645	650	655	
Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu			
660	665	670	

<210> 381

<211> 251

<212> DNA

<213> Homo sapien

<400> 381

ggagaagcgt ctgctggggc aggaagggtt ttccctgcc ttcacactgt ccctcaccaa	60
ggtaacatgc ttcccctaag ggtatccaa cccaggggcc tcaccatgac ctctgagggg	120
ccaatatccc aggagaagca ttggggagtt gggggcaggt gaaggaccca ggactcacac	180
atccctggcc tccaaggcag aggagagggt cctcaagaag gtcaggagga aaatccgtaa	240
caagcagtca g	251

<210> 382

<211> 3279

<212> DNA

<213> Homo sapiens

<400> 382

cttcctgcag cccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa	60
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<210> 383

<211> 154

<212> PRT

<213> Homo sapiens

<400> 383

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Gly Lys Arg Gly Pro Leu Leu Gln Gly	Leu Thr Trp Ala Thr Gly Gly	
20	25	30

His Cys Phe Ser Ser Glu Glu Ser Gly	Ala Val Asp Gly Ala Gly Gln	
35	40	45

Lys Lys Asp Arg Ala Trp Leu Arg Cys	Pro Glu Ala Val Ala Gly Phe	
50	55	60

Pro Leu Gly Ser Asp Cys Arg Glu Gly	Gly Arg Gln Gly Cys Gly Gly		
65	70	75	80

Ser Asp Asp Glu Asp Asp Leu Gly	Val Ala Pro Gly Leu Ala Pro Ala	
85	90	95

Trp Ala Leu Thr Gln Pro Pro Ser Gln	Ser Pro Gly Pro Gln Ser Leu	
100	105	110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln	Trp Val Ile Leu Ile Thr	
115	120	125

Glu Leu Thr Ile Pro Ser Pro Ala His	Gly Pro Pro Trp Leu Pro Asn	
130	135	140

Ala Leu Glu Arg Gly His Leu Val Arg	Glu
145	150

<210> 384
<211> 557
<212> DNA
<213> Homo sapiens

<400> 384
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ggggaaagggt cccttttgc ttcgccaagtg ccataaccat gaggactact ctaccatgg 180
tctgcctctt ggccaaggcg gctggttgc aagaatgaaa tgaatgattc tacagctagg 240
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ccttcttatt tatgtgaaca actgtttgtc ttttttgc tctttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540
aaaaaaaaaaaaaaa 557

<210> 385
<211> 337
<212> DNA
<213> Homo sapiens

<400> 385
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tctcaagcc atctgtgtc ttcgagtagc gacacatcat cactcctgc ttgtgtatca 180
aaacgtggag gtgttttcc tcagctaaga agcccttagc aaaagctgca atagacttag 240
tatcagacag gtcagtttc cgccaccaaca cctgctgggtt ccctgtcgtg gtctggatct 300
cttggccac caattcccccc tttccacat cccggca 337

<210> 386
<211> 300
<212> DNA
<213> Homo sapiens

<400> 386
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gcccgcctcg cccagagggt gggcgccggg ctgcctctac cggctggcggt ctgttaactca 120
gcgcaccttgg cccgaaggct ctagcaagga cccaccgc accccgcggg cggccggcgc 180
gcggactttg cccgggtgtgt ggggcggagc ggactgcgtg tccgcggacgc ggcacgcgaag 240
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<210> 387
<211> 537
<212> DNA
<213> Homo sapiens

<400> 387
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cccccttcctg tgccatcatg atcagcacct atgatgttgc caaaagcttc ttccagaggc 120
tgaaccagga cccgcttctg ggcggctgaa aggggcagg aggcaaggac cccgtctctc 180
ccacggatgg ggagagggca ggaggagacc cagccaaatg ccttttcctc agcactgagg 240
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gcggcccagc acttcctcag acacaacttc ttctgtgtc tccagtcgtg gggatcatca 360
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gtttgtgtt gctgggcattt tctccaggaa ccaagaagcc ctcagctgg ttttttttttgc 480
ctgacccttg ttaatttcattt aagtctaaag atgatgaact taaaaaaaaaaaaaaa 537

<210> 388
<211> 520
<212> DNA
<213> Homo sapiens

<400> 388
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tgaggttaaa ccagtttgc a ttccccat gtggaaaaag taaggaggact actcagcact 120
gtttgaagat tgccttct acagttctg agaattgtgt tatttcattt gccaagtcaa 180
ggacccctc cccaaatgc cccagccac ccctaagcat ggtccctgt caccaggcaa 240
ccagggaaact gctacttgc gacccatcca gagaccagga gggtttgggt agctcacagg 300
acttccccca ccccagaaga ttagcatecc atactagact cataactcaac tcaacttaggc 360
tcatactcaa ttgatggta ttagacaatt ccatttctt ctggttatta taaaacagaaa 420
atcttcctc ttctcattac cagtaaaggc tcttggtate tttctgttgg aatgattct 480
atgaacttgt ctatattaa tggtgggtt ttttctgg 520

<210> 389
<211> 365
<212> DNA
<213> Homo sapiens

<400> 389
cgttccccca gtttgacaga agggaaaggcg gagcttattc aaagtctaga gggagtggag 60
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aacgactttc caaataatct caccagcgcc ttccagctca ggctccctag aagcgtctt 180
aagcctatgg ccagctgtct ttgtgttccc ttcacccgc ctgtccctac agctgagact 240
cccaaggaaac cttcagacta ctttcctctg cttcagccaa ggggcgttgc ccacattctc 300
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gggag 365

<210> 390
<211> 221
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G

<400> 390
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gtctctangag tctganncga ntcggtgccc cantntgaca naaggaaagg cgagcttat 180
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<210> 391
<211> 325
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G

<400> 391

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 tagccaggc actgctgcca acagccagtc cnatnacat catgtnaccc ggtgnctct 180
 naantngat ntccanagcc ctaccatcn tagttctgtct ctcccacccg ntaccagccc 240
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 gagacctccg getactacta tgacc 325

<210> 392
 <211> 277
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(277)
 <223> n = A,T,C or G

<400> 392
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 agtctcaactt nggcnagnngn ctccctacttg agtctcttcc cccgcctgnn ccagtngnaa 120
 antaccanga accgnatgn cttanaacn ncctgggtnn tgggtnntc aatgactgca 180
 tgcagtgcac caccctgtcc actacgtgat gctgttaggat taaaagtctca cagtgccgg 240
 ctgaggatac agcgccgcgt cctgtgtgc tgggaa 277

<210> 393
 <211> 566
 <212> DNA
 <213> Homo sapiens

<400> 393
 actagtccag tgggtggaa ttgcggccg cgtcgacgga caggtcagct gtctggctca 60
 gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga taaaattcag cctaaacgtt 120
 ttgcgggaa cactgcagag acaatgctgt gagttccaa ccttagccca tctgcgggca 180
 gagaaggtct agtttgtcca tcagcattat catgatatca ggactggta cttgtttaag 240
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 ttttgcctat caaaaaaaaaa aaaaaaa 566

<210> 394
 <211> 384
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(384)
 <223> n = A,T,C or G

<400> 394
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tgagcagatg gtttctgagg acgt 384
 <210> 395
 <211> 399
 <212> DNA
 <213> Homo sapiens
 <400> 395
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 <210> 396
 <211> 403
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(403)
 <223> n = A,T,C or G
 <400> 396
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 agacaaggac aacctgttcc ttcat'aactc tctagagaaa aaaaggagtt gtttagtagat 180
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 gtttagggga gggagtgagg gataaaagaa ggaaaaaaaaaag aagagtgaga aaaccttattt 360
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 <210> 397
 <211> 100
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(100)
 <223> n = A,T,C or G
 <400> 397
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 tccatccccg ctctgggtt gtnacagaat gactgacaaa 100
 <210> 398
 <211> 278
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(278)
 <223> n = A,T,C or G

<400> 398

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ccacctggac atcttggaaat cagcggcctg gatgaaaagag cggacttac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggatgg actcatcatg 180
ctccgggcag cccatccacc tttggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcatttangt ggctcaacaa ggagaagg 278

<210> 399

<211> 298

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(298)

<223> n = A,T,C or G

<400> 399

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gggggtccng catggagcgc atggggcgg gcctgggcca cggcatggat cgcgtggct 120
ccgagatcga ggcatgggc ctggatcatgg accgcatggg ctccgtggag cgcattggct 180
ccggcattga ggcatgggc cgcgtggcc tcgaccacat ggctccanc attgancgca 240
tggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcattggg 298

<210> 400

<211> 548

<212> DNA

<213> Homo sapiens

<400> 400

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gtacatgtac atgtatgaaa tttcccttc ttaccgaact ctctccacac atcacaagg 120
caaagaacca cacgcttaga aggtaagag ggccacctat gaaatgaat ggtgatttct 180
tgagtcctt tttccacgt ttaaggggatc atggcaggac ttagagtgc gagtaagac 240
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ctttccatgt atcttctacc atggccccc ctcctggat caagcccttc ccaggccctg 480
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agcaggat 548

<210> 401

<211> 355

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(355)

<223> n = A,T,C or G

<400> 401

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taagagtggt ggcctatattc agctgtttt acaaaatgac tggctctga cttaacgttc 180
tataaatgaa tttgtgttggaa caaaatgtccc atggggcgaa cgaagaagan aaagatgtgt 240
tttgggggggg actctctgtg gtccttcca atgttggggg tttccaaacca gggggagggt 300

cccttttgc a ttgccaagt g ccataaccat gagcactact ctaccatgg n tctgc 355
<210> 402
<211> 407
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(407)
<223> n = A,T,C or G

<400> 402
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aaatggaaaa cagaaaaaaag caggtgttgc actcctactt tctgacaaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacccctt ataaatctca 240
ttgcttgata ccaacctggg ctgtttaat tgcccaaacc aaaaggataa tttgctgagg 300
tttgtggagct tctccccctgc agagagtccc tgatctccca aaatttggtt gagatgtaaag 360
gntgattttg ctgacaactc ctttctgaa gtttactca ttccaa 407

<210> 403
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 403
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tagagaacaa gacctactca gtcataaca aaaaaggcaga caccacatg gatctcatgg 180
gggattggat attgttaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcgtaac catgtgaaa 300
gga 303

<210> 404
<211> 225
<212> DNA
<213> Homo sapiens

<400> 404
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attgttaatg cactcattt cctttacatg gtggaaagtcc tctcttgatc ctacaaacac 120
acattttcca ctctgtttc catagtttt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaaagtgc ctgtgtataa aataaagtat ctttatttca ttcat 225

<210> 405
<211> 334
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

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tcatccccat cccatgc caa aggaagaccc tccctcctt gtcacagcc ttctcttaggc 180
ttcccagtgc ctccaggaca gagtggtta tggtttcagc tccatcctt ctgtgagtgt 240
ctggtgcggt tgcctcca gcttctgtc agtgcttcat ggacagtgtc cagcccatgt 300
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<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

ttcataacct aatgagggag ttganatnac atnnaaccag gaaatgcatt gatctaang 60
gaaacaaaca cccaataaaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaaacaca aatttnatgt tgcaccctt tttctacacc tgtgggttat gacaaagaca 180
actgccaag aatnttcaag aaggaggact gccant 216

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

gctgacttgc tagtattcatc tgcattcatt gaagcacaag aacttcattgc cttgactcat 60
gtaaatgc aa taggattaaa aaataaattt gatattcat gaaaaacagac aaaaaatatt 120
gtacaacatt gcacccagtgc tcagattcta caccggcca ctcaggaaagc aagagttat 180
cccagggc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gataacttatt cacatttcat atggcaacc 300
tgccagacag gagaaagtct tccatgtta aaagacattt attatctgt tttctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgttagta aag 413

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

ggagctngcc ctcatttcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gtaatcctt aaaggctan ntaatcctt actagtccct ccatgtgag 120
cattatcctt ccagtattcn cttctnttt tatttactcc ttcctggcta cccatgtact 180
ntt 183

<210> 409

<211> 250

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G

<400> 409
cccacgcatg ataagctt tatttctgt a gtcctgcta g gaaaatcatc a aatctgacg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gcccccagga c agcgtggc tatgtttaca ggcntcctt gctggggggg 240
ggcncntatgc 250

<210> 410
<211> 306
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G

<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgc aa tcccatattgc aggatccgctc t tgcacatg cctctgtaga gagcagcatt 120
cccagggacc ttggaaacag ttggactgt aagggtcttgc tcccccaaga cacatccaa 180
aagggtgtgt aatggtaaa accgcttcc tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ct tttttgn atcttttta aactggaaag ttcaattngaaaatgaata 300
tcntgc 306

<210> 411
<211> 261
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G

<400> 411
agagatattt ctttaggtt a a gttcataga gttccatga actatatgac tggccacaca 60
ggatctttt g tttttttt gttttaagg a ttctgagatt ttgcttgc aggatttagat aaggctgttc 120
tttaaatgtc t gaaatggaa cagattcaa aaaaaaacc cacaatctag ggtggaaaca 180
aggaaggaaa gatgtgaata ggctgtatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa g gngaggcaa a 261

<210> 412
<211> 241
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt ctgcggcagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggagggag 180
ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

aactttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttcttagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tcctcatttg gaacctaaaa actctttct tcctgggtct gagggctcca 180
agaatccttg aatcatttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccaactctgtc ctggaggcac tggaaagcct agagaaggct 120
gtgagccaag gagggagggt cttcctttgg catggatgg ggtatgaagta aggagaggga 180
ctggaccccc tggaaagctga ttcaactatgg gggaggtgt attgaagtcc tcca 234

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

gcataggatt aagactgagt atctttcta cattttta actttctaag gggcacttct 60
caaaacacag accaggtacg aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>

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<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagcttt tgattcccg aatcaagaac tctcccttc agactattac 120
cgaatgcaag gtggtaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atatttggAAC agatggagtc tctactaca aag 213

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtggaaagg ctttactctg agttcaaatac ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtggttggaa agagcttcag gagggatccc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaaatg tgagatatgt gggaaaggct 240
tcantcaaag ttcgttatctt caaatccatc ngaaggncca cagttananaa aaccctttt 300
agt 303

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 418
tttttggcgg tgggtggggca gggacgggac angagtctca ctctgttgc caggctggag 60
tgcacaggca tgatctcgcc tcactacaac ccctgcctcc catgtccaag cgattttgt 120
gcctcagccct tccctgttagc tagaattaca ggcacatgcc accacacccca gctagtttt 180
gtatTTTtag tagagacagg gtttccatc gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagccccc 300
aaagtgtctt gattacaggc cgtgagcc 328

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60
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acccctgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
 cttgttcct ctctgtggct ccattcatag cacagttgtt gcactgagge ttgtgcaggc 180
 cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacagg gtgccaggca 240
 ccggttctcc agccacccaac ctcactcgct ccogccaaatg gcacatcaagt tcttctaccc 300
 taaagtagg accaaaaggc atctgcttt ctgaagtccct ctgctctatc agecatcacg 360
 tggcagccac tcnggctgtc tcgacgcgg 389

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

gttcctcccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
 tggccaggc agcaaggcctt agcctggct tcttgcctt gcttttttc tggcttagacc 120
 gaagtgtact agccaaggag ttgaagttt tgacttttgtt gtttcggcat ggagaccgaa 180
 gtcccatgtt cacccttccc actgaccca taaaggaatc ctcatggcca caaggattt 240
 gccaactcac ccagctggc atggagcage attatgaact tggagagttataataagaaaga 300
 gatataaaaa attcttgaat gatccctata aacatgaaca gtttatattt cgaagcacag 360
 acgttgcaccg gactttgtatg aagtgcatac acaaacctgg caagcccg 408

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

gctaaaaat cttttactg atnngcatgg ctacacaatc attgactatt acggaggcca 60
 gaggagaatg aggctggcc tggagccct gtgcctacta naagcacatt agattatcca 120
 ttcactgaca gaacaggctt tttttgggtc ctctttctcc accacnataat acttgcagtc 180
 ctcccttctt aagattctt ggcagtgtc ttgtcataa cccacagggt tagaaacaag 240
 ggtgcacat gaaatttctg ttctgttagca agtgcatgtc tcacaagggtt gcangtctgc 300
 cactccgagt ttattgggtg ttgtttccct ttgagatcca tgcatttcct gg 352

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

atgccaccaat gctggcaatg cagcggcggt tcgaaggcct gcatatccag cccaaagctgg 60
 cgatgatcga cggcaaccgt tgccccaaatg tgccgatgcc agccgaagcg gtggtaagg 120
 gcgatagcaa ggtgcggcg atcgcggcg ctgtcaatccct ggccaagggtc agccgtgatc 180
 gtgaaatggc agctgtcgaa ttgtatctacc cgggttatgg catcggcgaaa cataagggt 240
 atccgacacc ggtgcacctg gaagccttgc agccgtggg gcccacgccc attcaccgac 300
 gcttctcccg ccggtaacggc tggcctatga aaattat 337

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G

<400> 423
gctaaaaat cttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgccctactan aagcncatta gattatccat 120
tcactgacag aacaggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattcttg gcagttgtct ttgtcataac ccacagggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgttagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta 310

<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(370)
<223> n = A,T,C or G

<400> 424
gctaaaaat cttttactg atagggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacatcg attatccatt 120
caactgacaga acaggtcttt tttgggtcc ttcttctccac cacgatatac ttgcagtcc 180
ccttcttga gattcttgg cagttgtct ttgtcataacc cacaggtgt aaaaacatcct 240
ggtaatct cctggaaactc cctcattagg tatgaaatag catgatgcat tgcataaaagt 300
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcatgtga taagcaggac 360
tccgtcgacg 370

<210> 425
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 425
aattgctatn ntnttattttg ccactaaaa taattaccaaa aaaaaaaaaa ntntaaatga 60
taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatngggcga 120
anattatcca ttatnttaag ggttgaactc aggtacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtntntg aggagg 216

<210> 426
<211> 596
<212> DNA
<213> Homo sapiens

<400> 426
cttccagtga ggataaccct gttgccccgg gcccgggttc tccattaggc tctgattgat 60
tggcagtca g tggatggagg gtgttctgat catccgact gccccaaagg tcgctggcca 120
gctctctgtt ttgtcgatgg ggcgttagga cctaatttgt taattaagag tagatggta 180
gctgtccttg tattttgatt aacctaattgg ccttcccagc acgactcgaa ttccagctgga 240
gacatcacgg caactttaa tggaaatgatt tggaaaggcca ttaagaggca cttcccgta 300

ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggctttt gtttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc ctttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctggagcc cgtgtct 596

<210> 427
<211> 107
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A,T,C or G

<400> 427
gaagaattca agttaggttt attcaaaggg cttaacngaga atcctanacc caggncccag 60
cccgaggaca gccttanaga gctcctgttt gactgcccgg ctcagng 107

<210> 428
<211> 38
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(38)
<223> n = A,T,C or G

<400> 428
gaacttccna anaangactt tattcactat tttacatt 38

<210> 429
<211> 544
<212> DNA
<213> Homo sapiens

<400> 429
ctttgctgga cggaaaaaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcgggtca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcggt 240
gccttccact tcagttacac ctcactcacc atccctctctt gttggttctg tgctgcttca 300
agatactaag cccacattt agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgcccttta tgatgtcctt gatgttctca tcaagcccc 420
gagtttagtt caaaggcagta ttccaggatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gtttagagaga tatgcataatc caggatttt ttgccagggtg gttaggagaga 540
ttat 544

<210> 430
<211> 507
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(507)

<223> n = A,T,C or G

<400> 430

cttatcnaaa tggggctccc aaacctggct gtgcagtggaa aactccgggg gaattttgaa 60
 gaacactgac acccatcttc caccggaca ctctgattt attggctgc agtgagaaca 120
 gagcatcaat taaaaaagct gcccagaatg ttntcctggg cagcgtgtg atcttgcen 180
 ccttcgtgac ttatgcaat gcatcatgct atttcataacc taatgaggga gttccaggag 240
 attcaaccag gatgtttcta cnccctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
 caagaaggag gactgcaagt atatcggtt ggagaagaag gacccaaaaa agacctgttc 360
 tgtcagtggaa tggataatct aatgtcttc tagtaggcac agggctcca ggcaggcct 420
 cattctccctc tggcctctaa tagtcaatga ttgtgttagcc atgcctatca gtaaaaagat 480
 tttttagcaa aaaaaaaaaaaaaaaa aaaaaaaaaaaa 507

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

gaaaattcag aatggataaaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
 aaacaagaaa gcacttatca ggaggactta caaatggaaag tacactctan aaccatcatc 120
 tatcatggct aaatgtgaga ttagcacagc tgattattt gtacattgca aacacctaga 180
 aagagatggg aaacaaaatc ccaggagttt tgggtgtggaa gtcctgggtt ttccaacaga 240
 catcattcca gcattctgag attagggnga ttgggatca ttctggagtt ggaatgttca 300
 acaaaaagtga tgggtttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
 gcaatgagtc tggctttac tctgctgtttt ct 392

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
 aaatgcaagg caacatgtgt agatctcttgc tcttattttt ttgtctataa tactgtattt 120
 ngtatccaa gctctcggnna gtccagccac tgngaaacat gctcccttta gattaacctc 180
 gtggacnctn ttgttgnattt gtctgaactg tagngccctg tattttgtt ctgtctgnga 240
 attctgttgc ttctggggca ttcccttgng atgcagagga ccaccacaca gatgacagca 300
 atctgaatttgc ntccaaatcactc agctgcgatt aagacataact gaaatcgatc aggaccggga 360
 acaacgtata gaacactgga gtcctttt 387

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (281)
<223> n = A, T, C or G

<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactata 120
caggcnctat ttgggttggc tggaggagct gtgaaaaca tggagagatt ggcgctggag 180
atgcgcgtgg ctattcctcn ttgnattac accagngagg ntctctgtnt gcccaactgg 240
tnnaaaaccg ntataacaata atgatagaat aggacacaca t 281

<210> 434
<211> 484
<212> DNA
<213> Homo sapiens

<400> 434
ttttaaaata agcatttagt gctcagtccc tactgagttac tctttctctc ccctcctctg 60
aatttaattc ttcaacttg caatttgc当地 ggattacaca tttcaactgtg atgtatattg 120
tgttgcaaaa aaaaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttccccca ttggaacttag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtc当地 tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484

<210> 435
<211> 424
<212> DNA
<213> Homo sapiens

<400> 435
gcgcgcgtca gaggcaggta ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
ggtagctt caatatcgca ggttcttaact cctctgcctc tataagctca aaccaccaa 120
cgatcgccca agtaaaccggc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggggggggg caagatagat gggggggggc ggcattggcgc ggggtgaccc 240
cttggagaga gggaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggttagagacc ttggggggtc tgaaacctct ggactccccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggatttc tctgttttc actegcaata aattcagagc 420
aaac 424

<210> 436
<211> 667
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1) ... (667)
<223> n = A, T, C or G

<400> 436
accttggaa nactctcaca atataaaggc tcgttagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagtttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctttctt ggaattcctc tgatttcaaa gtctcaactt caagttcttggaaaacgagg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggtcgcc agagtagggat aggattccag atgctgacac cttctggggg aaacagggtct 300
gccaggtttg tcatagcaact catcaaagtc cggtcaacgt ctgtgcttcg aatataaacc 360

tgttcatgtt tataggactc attcaagaat tttctataat tctttcttat atactctcca 420
 agttcataat gctgctccat gcccaagctgg gtgagttggc caaatcctt tgcccatgag 480
 gattcctta tggggctagt gggaaagggtg tcaatgggc ttcggctc atgcccggaaac 540
 accaaaagtca caaacttcaa ctccctggct agtacacttc ggtctagcca gaaaaaaagc 600
 agaaaacaaga agccaaggct aaggcttgcg gccctgccag gaggaggggt gcagctctca 660
 tgttag 667

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

ctacgtctca accctcattt ttaggttaagg aatcttaagt ccaaagatat taagtgactc 60
 acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggtttgt 120
 taaagctcag gtttaggggc tgataagctt ggaaggaact tcagacagct tttcagatc 180
 ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
 aggtactctt ctatttcac ccctcttgcg tctactctct ggcagtcaga cctgtggag 300
 gccatgggag aaagcagctc tctggatgtt tgtagacate atggactatt ctctgtggac 360
 catttctcca ggttacccta ggtgtacta ttggggggac agccagcata tttagcttc 420
 atttgagttt ctgtctgtct tcagtagagg aaactttgc tcttcacact tcacatctga 480
 acacctaact gctgttgctc ctgagggtt gaaagacaga tatagagctt acagtattta 540
 tcctatttctt aggcaactgag ggctgtgggg taccttgcg tgccaaaaca gatcctgttt 600
 taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgtt gctctttacc 660
 ctgcatcatg tgctctttgc gctgaaaatg acc 693

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

ctgcttatca caatgaatgt tctcctggc agcgttgtga tctttccac cttcgact 60
 ttatgcaatg catcatgcta tttcataacct aatgaggggag ttccaggaga ttcaaccagg 120
 atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatctt aagaaggagg 180
 actgcaagta tatctgggtt agaagaagga cccaaaaaaag acctgttctg tcagtgaatg 240
 gataatctaa tttgtctca gtggcacag ggctcccagg ccaggcctca ttctcctctg 300
 gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 439

gttcctnnnta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctctcc 60
 tggccagggc agcaaggcctt agccttgcg tcttgcgtt gcttttttc tggctagacc 120
 gaagtgtact agccaaggag ttgaagtttgc tgactttggt gtttcggcat ggagaccgaa 180
 gtccccatttgc cacccccc actgacccca taaaggaatc ctcatggcca caaggatttgc 240
 gccaactcactc ccagctggc atggagcagc attatgaact tggagagttt ataagaaaga 300
 gatataaaaa attcttgcgat gacttgcata aacatgaaaca ggtttatattt cgaagcacag 360
 acgttgaccg gactttgcg tggctatgc caaacctggc agcccgctga cgccggcccg 420
 aatttagtag t 431

<210> 440
<211> 523
<212> DNA
<213> Homo sapiens

<400> 440
agagataaaag ctttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttgc tatttaagga ttctgagatt ttgcttgagc aggatttagat aaggctgttc 120
tttaaatgtc taaaaatggaa cagattcaa aaaaaaaaccc cacaatctag ggtggaaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaaacca atttaccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctgaa agtttctcc 300
actggaaaac tgctactata tggtttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctcttg tgcctttgg tcctggaaaca tttatgtcc tttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatacgca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta 523

<210> 441
<211> 430
<212> DNA
<213> Homo sapiens

<400> 441
gttccctccta actcctgccaa gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccaggggc agcaaggcctt agccttggct tcttggttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttgc tgactttgggt gtttcggcat ggagaccgaa 180
gtccccatttgc cacccttccc actgacccca taaaggaatc ctcatggccca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagat ataagaaaaga 300
gatataaaaa attcttgaat gatgcctata aacatgaaca gttttatatt cgaagcacag 360
acgttggccggc gactttgtatgc agtgcctatgc caaacctggc agcccgctgca cgcggccg 420
aatttagtag 430

<210> 442
<211> 362
<212> DNA
<213> Homo sapiens

<400> 442
ctaaggaaatt agtagtgttc ccatcacttgc tttggagtgt gctattctaa aagattttga 60
tttccctggaa tgacaattttt atttaactt tggggggggaa aagagttata ggaccacagt 120
cttcaacttctt gatacttgcata aattaactttt ttattgcact ttttttttttttgcattt 180
atgttttagaa atggtcatttt tacggaaaaaa tttagaaaaat tctgataata gtgcagaata 240
aatgaattaa ttgttttactt aattttatattt gaactgtcaa tgacaaataaa aaattttttt 300
tgattttttt ttgttttcat ttaccagaat aaaaactaag aattaaaatgtt ttgattacag 360
tc 362

<210> 443
<211> 624
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G

<400> 443
ttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60

ttgaaagaat taaaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
 aatgcttatt taaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgcctttg 180
 tgctggctag tactccgtc ggtgtcagca gcacgtggca ttgaacattt caatgtggag 240
 cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttccctgttt 300
 tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc taaaatgaac 360
 taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatttggtag 420
 atgttaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtc atatgcta 480
 agtacagaga gagggcactt aaaccaacta agggcctgga gggaaagttt cctggaaaga 540
 ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tattttaact 600
 ttgtccctat ctgctaaaca gatc 624

<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

<400> 444
gcacatcatt nntcttgcat tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgtttgc ttagaaatag aacaagtaag 120
ttcattgtca tagcataaca caaaatttgc ataagtgggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgcacac tctaactccc tgaatgtttt 240
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cctctgcaat ctgccaccc ctgctggcag gatttgggg tgcatecctgt gaagagccaa 360
ggagggcacca gggcataagt gagtagactt atggtegacg cggccgcgaa ttttagtagta 420
gtaga 425

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

<400> 445
catgtttatg ntttggatt actttggca cctagtgttt ctaaatcgac tatcattttt 60
ttctgtttt caaaagcaga gatggccaga gtctcaacaa actgttatctt caagtctttg 120
tgaaattttt tgcattgtggc agattattgg atgtatctt ctttaacttag catataaaatc 180
tgggtgtttt cagataaaatg aacagaaaaa tgggtggaa ttaccatttg gaacattgtg 240
aatggaaaaat tggctctta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaattgtactt aggttctcc tcttgttatt tgaagcagtg 360
tgggtgtggc attgataaaa aaaaaaaaaaag tcgacgcggc cgccgaaat ttaaattttt 414

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(631)

<223> n = A,T,C or G

<400> 446

acaaattaga anaaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgcga ggagccatct tgcaagggtg 120
atgctggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
ccggccatgt acgatttcag tatgtctta tcgcagctgt gattggaaaca atttagattg 240
ctgtcatctg tgggtggtc ctctgcatca caagggccaa actttagta atagcattgg 300
actgagattt gtaaaacttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttggc ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tggccttg catttgtgtt 540
aatctacacc aatgaaaaca tgtactacag ctatattga ttatgtatgg atatattga 600
aatagatac attgtcttga tgtttttct g 631

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

ccttggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaagg 60
cctggccatg taatcctgaa agtttccca aggttagctat aaaatcctta taagggtgca 120
gcctttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgaggc 180
agttcctgaa aggccaggat agcaactgtat cttcagaaag aggaactgtg tgcaccgg 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tggcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatcctgtt ggcctgagg 480
attcctttat ggggtcagtg ggaaagggtt caatggact tgggtctcca tgccgaaaca 540
ccaaagtacaa aacttcaac tccttggcta gtacacttcg gtcta 585

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

tgctcggtt tcattctgan nnccgaactg accntgccag ccctgccan gggccnccat 60
ggctccctag tggccctggag aggangggc tag 93

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(706)
 <223> n = A,T,C or G

<400> 449

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ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggctggcg cgtcccattc gccattcagg ctgcgcact 240
gttgggaagg gcgatcggtg cgggcctt cgttattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tggtaacgc cagggttttc ccagtcnnga cggtgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct ctagagcgcg cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
caactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggcttag 600
aacaggttga acctggggagg tggagttgc aatgagctga gatcaggccn ctgcncccc 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaaa 706
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<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

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gagacggagt gtcactctgt tgcccaggct ggagtgcgc aagacactgt ctaagaaaaa 60
acagtttaa aaggtaaaac aacataaaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaaggatc ttacagacat gtcgccaata tcactgcattg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaagg tggaaatgg gttttttttt actcaaattt atccctgcac ctgaaacgc 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagtctta aaccacttgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactccat tgccgggggt cgacgcggcc 480
gcgaatttag tag 493
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<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 451

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gggcgcgtcc cattcgccat tcaggctgca caactgttgg gaagggcgat cggcgccggc 60
ctttcgta ttacgcgcgc tggcgaaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgcgcagg ttttcccgat cncgacgttg taaaacgcacg gccagtgaat tgaattttagg 180
tgacntata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atccctctaga 240
gcggccgcct actactacta aattcgccgc cgcgtcgacg tgggatccnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagactg agcagaagct ggaggccaaa 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttcaatga gctgagatca ggccnctgcn ccccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501
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<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A,T,C or G

<400> 452
agacggttc accnttacaa cncctttag gatgggnntt ggggagcaag c 51

<210> 453
<211> 317
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G

<400> 453
tacatcttgc ttttccccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaaccat 120
ttcacccana cagcctgttt ctatccctgtt taataaattt gtttgggtt tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac ttatTTTTC tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
tacccatgtc ttattttt 317

<210> 454
<211> 231
<212> DNA
<213> Homo sapiens

<400> 454
ttcgaggtac aatcaactct cagagtgttag tttccttcta tagatgagtc agcattaata 60
taagccacgc ca cgcttgc aaggagtctt gaattctcct ctgctactc agtagaaacca 120
agaagaccaa attcttctgc atcccagctt gcaaaacaaa ttgttcttct aggtctccac 180
ccttccttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455
<211> 231
<212> DNA
<213> Homo sapiens

<400> 455
tacaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acagggaaaca tgccaagttt 120
gttcaacgc attgatgact tctccaagga tcttccttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agtcacaaat acagggctcc ttttcctct a 231

<210> 456
<211> 231
<212> DNA
<213> Homo sapiens

<400> 456
ttggcaggtt cccttacaaa gaagacacca taccttatgc gttatttaggt ggaataatca 60
ttccattcag tattatcggtt attattctt gagaacccct gtctgtttac tgtaacctt 120
tgcactcaaa ttcccttatac aggaataact acatagccac tatttacaaa gccattggaa 180

ccttttatt tggcagct gctagtcagt ccctgactga cattgccaag t 231
<210> 457
<211> 231
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

<400> 457
cgaggtaccc aggggtctga aaatctctnn ttantagtc gatagaaaaa ttgttcatca 60
gcattccta atatgatctt gctataatta gatfffftc cattagagtt catacagttt 120
tatttgattt tatttagaat ctcttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggctttgt g 231

<210> 458
<211> 231
<212> DNA
<213> Homo sapiens

<400> 458
aggctctggtt ccccccacctt ccactccccct ctactctctc taggactggg ctgggccaag 60
agaagagggg tggtagggg agccgttgag acctgaagcc ccaccctcta ctttccttca 120
acaccctaac ttgggtaac agcatttggaa attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt gggggccag accccaggag aagaagatc t 231

<210> 459
<211> 231
<212> DNA
<213> Homo sapiens

<400> 459
ggtaccgagg ctcgctgaca cagagaaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ctttcgcgaa acctgtggtg gcccaccagt cctaacggga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagcc atccctgtccc tcattggctc tgtgtttcc 180
actatacaca gtcaccgtcc caatgagaaaa caagaaggag caccctccac a 231

<210> 460
<211> 231
<212> DNA
<213> Homo sapiens

<400> 460
gcaggatcaa catgctgcaa caacagatgt gacttaggaac ggccggtgac atggggaggg 60
cctatcaccc tattttggg ggctgtttct tcacagtgtat catgaagcct agcagcaat 120
cccacccccc cacacgcaca cggccagctt ggagccaca gaagggtcct cctgcagcca 180
gtggagctt gtcacccctc cagttccaccc ctaccaggct taaggataga a 231

<210> 461
<211> 231
<212> DNA
<213> Homo sapiens

<400> 461
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60

gcgttgctc cagaagagtg tggcatgcc agagggaaa caggcgctg tggccctgg 120
gtgggttca gtgaggagtg ggaaatttgt tcagcagaac caagccttg ggtgaataag 180
aggggatTC catggactg atagagccct atagttcag agctggaaAT t 231

<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

aggtaCCtC attgtagcca tggaaaatt gatgttcagt gggatcagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccataatctc atatgtatgt 120
gaagaactgt tagagagacc aacaggtag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatttaatt tcttctcaCT catccagtgt tggatTTAGG a 231

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

tactccagcc tggtgacaga gcgagaccct atcaccgccc cccacccac caaaaaaaaaa 60
actgagtaga cagggtcctt cttggcatgg taagtcttaa gtcCcCCTCCC agatctgtga 120
catttgcacag gttgttttc ctctggacct cggtgtcccc atctgatgtga gaaaaggcag 180
tggggagggtg gatcttccag tcgaagcggt atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

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aaggacatca catatgaaga atgttaagt tggaggtggc aacgtgaatt gcaaacagg 120
cctgcTTCAg tgactgtgtg cctgttagtcc cagctactcg ggagtctgtg tgaggccagg 180
ggtgcacgc caccagctag atgctctgtatc acttcttaggc cccattttcc c 231

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

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gtggcaaatt agcaacaaat tctgacatca tatttatggt ttctgtatct ttgtgtatga 120
aggatggcac aattttgtt tgtgttcata atatactcg attagttcag ctccatcaga 180
taaactggag acatgcaggaa cattaggta gtgtgttagc tctggtaatg a 231

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

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ggcCTCgaa cagaacttgc cacataccca ggtataatag tttctaatct ttgcccagg 120
cctgtcaat caaatattgt ggagaattcc ctagctggag aagtccaaaa gactataggc 180
aataatggag accagtcaca caagatgaca accagtcgtt gtgtgcggct g 231

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<210> 467  
<211> 311  
<212> DNA  
<213> Homo sapiens
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<400> 467

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tgtgccttaa cagaaggctc tgagattcta agtgggaatc atttcagtga ctgtcatgt 180
gcatgggtct ctgccaagc tcgtaatgag actatacgaa ggccggctgtg ggacgtcagt 240
tgtgacctgc tggccctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300
ctgcagcaga c 311

311

<210> 468

<211> 3112

<212> DNA

<213> Homo sapiens

<400> 468

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aagatctgca tggggaaag gacctgatga tacagagttt gataggagac aattaaaggc 120
tggaggcac tggatgcctg atgatgaagt ggacttcaa actggggcac tactgaaacg 180
atgggatggc cagagacaca ggagatgagt tggagcaagc tcaataacaa agtggttcaa 240
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aatgggata cacagtatga tctataaaagt gggatatagt atgatctact tcactgggtt 420
atttgaagga tgaattgaga taatttattt caggtgccta gaacaatgcc cagattagta 480
catttgggg aactgagaaa tggcataaca ccaaatttaa tatatgtcaag atgttactat 540
gattatcatt caatctcata gttttgtcat gcccccaattt atcctcaattt gtgcctcaac 600
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<211> 2426

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2426

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<211> 812

<212> DNA

<213> Homo sapiens

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<213> Homo sapiens

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<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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<213> Homo sapiens

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<223> n=A,T,C or G

<400> 475

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<211> 3434

<212> DNA

<213> Homo sapiens

<400> 476

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<210> 477
<211> 140
<212> PRT
<213> *Homo sapiens*

<400> 477
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His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His His Met Asp Thr
20 25 30

Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
35 40 45

His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
50 55 60

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
65 70 75 80

Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
85 90 95

100 105 110

115 120 125

130 135 140

<211> 143
<212> PRT
<213> *Homo sapiens*

<400> 478

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
5 10 15

Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
20 25 30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65 70 75 80

His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
100 105 110

Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
115 120 125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
130 135 140

<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
5 10 15

Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
20 25 30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
100 105 110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
115 120 125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
130 135 140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
145 150 155 160

Cys His Thr Asp Thr Thr Ser Leu Pro His Phe His Val Ser Ala
165 170 175

Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
180 185 190

Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
195 200 205

Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
210 215 220

<210> 480
 <211> 144
 <212> PRT
 <213> Homo sapiens

<400> 480
 Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
 5 10 15
 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
 20 25 30
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
 35 40 45
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
 50 55 60
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
 65 70 75 80
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
 85 90 95
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
 100 105 110
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
 115 120 125
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
 130 135 140

<210> 481
 <211> 167
 <212> PRT
 <213> Homo sapiens

<400> 481
 Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
 5 10 15
 Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
 20 25 30
 Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
 35 40 45
 Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
 50 55 60
 Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro

65	70	75	80
Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg			
85		90	95
Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala			
100		105	110
Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His			
115		120	125
Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe			
130		135	140
Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser			
145		150	155
Trp Leu Ser Arg Gly Arg Pro			
165			

<210> 482
<211> 143
<212> PRT
<213> Homo sapiens

<400> 482			
Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val			
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Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu			
20		25	30
Arg Ala Ser Trp Leu Pro Gly Gly Pro Gln Ala Ile Leu Gly Arg			
35		40	45
Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly			
50		55	60
Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe			
65		70	75
80			
Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr			
85		90	95
Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly			
100		105	110
Ala Ser Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys			
115		120	125
Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly			
130		135	140

<210> 483
<211> 143
<212> PRT

<213> Homo sapiens

<400> 483

Met	Glu	Thr	Gln	Arg	Gly	Asn	Lys	Gln	Arg	Ala	Gln	Glu	Gln	Gly	Val
				5					10					15	

Cys	Cys	Leu	Trp	Gly	Ser	Ser	Pro	Cys	Leu	Gly	Ser	Tyr	Gly	Thr	Ala
				20				25						30	

Gly	Phe	Leu	Val	Ala	Lys	Arg	Arg	Thr	Thr	Gly	Leu	Leu	Glu	Glu	Asp
				35			40					45			

Phe	Thr	Phe	Lys	Cys	Arg	Lys	Gln	Pro	Lys	Leu	Pro	Ser	Met	Arg	Leu
		50			55					60					

Ser	Leu	Leu	Trp	Pro	Trp	Arg	Asp	Leu	Lys	Phe	Val	Pro	Arg	Gln	Asp
	65				70				75				80		

Lys	Leu	Thr	Arg	Ser	Ser	Val	Ser	Val	Ala	Gly	Ala	Tyr	Ala	Cys	Arg
	85							90				95			

Ala	Gly	Pro	Gly	Trp	Leu	Lys	Glu	Gln	Pro	Ala	Thr	Ser	Ala	Arg	Val
	100					105					110				

Arg	Leu	Val	Gln	Ala	Glu	His	Pro	Pro	Pro	His	Pro	Leu	Glu	Glu	Val
	115					120					125				

Gly	Met	Ala	Arg	Phe	Pro	Gln	Pro	Glu	Cys	Leu	Pro	Pro	Tyr	Cys
	130				135				140					

<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

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	20				25				30					

<210> 485

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

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<210> 486

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 486
gcgaattctc acgctgagta tttggcc 27

<210> 487
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 487
cccgaaattct tagctgccca tccgaacgcc ttcatc 36

<210> 488
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 488
gggaagcttc ttccccggct gcaccagctg tgc 33

<210> 489
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 489
Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
1 5 10 15
Ser Val Ala

<210> 490
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
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<400> 490
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
1 5 10 15
Leu Ser His Ser
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<210> 491
<211> 20
<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
1 5 10 15
Thr Gly Phe Thr
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<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala Leu Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr
1 5 10 15
Leu Ala Ser Leu
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<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr Thr Leu Ala Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro
1 5 10 15
Lys Tyr Arg Gly
20

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu Pro Lys Tyr Arg Gly Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser
1 5 10 15
Leu Met Ile Ser
20

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 495
Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro
1 5 10 15
Phe Pro Asn Gly
20

<210> 496
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 496
Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1 5 10 15
Pro Pro Pro Pro Ala
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<210> 497
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 497
Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
1 5 10 15
Ser Val Arg Val
20

<210> 498
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 498
Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val
1 5 10 15
Val Pro Gly Arg
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<210> 499
<211> 20
<212> PRT
<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 499

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Ser	Ala	Phe	Leu												
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<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

Leu	Asp	Ser	Ala	Phe	Leu	Leu	Ser	Gln	Val	Ala	Pro	Ser	Leu	Phe	Met
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Gly	Ser	Ile	Val												
			20												

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

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Val	Ser	Ala	Ala												
			20												

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 502

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ctgt	agat	tttggatng	acctca	caatgc	agctgggtcc	gccaggctcc	180
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gaa	agg	ccga	ttnatnatt	ccaaaacctn	gaccacggtg	tgaccagtcc	300
gac	acc	gag	catttttg	cctatttttg	tggcagaatg	aatactgta	360
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				gcaccctggt	tcaggcaac	ctaa	414

<210> 503

<211> 379

<212> DNA

<213> Homo Sapiens

<220>

<221> misc_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

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a gctatggag t gtagctgggt c cggcaggct ccagggaaagg ggctgnata catcgatca	180
t tagtagtag t ggtacattt tacgcgagct gggcgaaaagg ccgattcacc atttccaaaa	240
c ctngaccac ggtggatttg aaaatccaca gttgacaac cgaggacacg gccacctatt	300
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t ntcttagg gcaacctaa	379

<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu			
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Asn Ser Ala			

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr			
1	5	10	15
Asn Thr Ala Asn			
20			

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

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accgtctctg gattctccc t cagtagcaat gcaatgatct gggtccgcca ggctccaggg	180
a a ggggctgg aatacatcg atacattagt tatggtgta ggcatacta cgcgagctgg	240
gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt	300
ctgacaaccg aggacacggc cacatttc t gtcgacccaa atatgtattt tagtggtatg	360
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<210> 507
<211> 422
<212> DNA
<213> Homo Sapien

<400> 507
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aa 422

<210> 508
<211> 411
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (1)...(411)
<223> n = A,T,C or G

<400> 508
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cagtcctctgg aatcgaccc tcgatgtact gcatgagctg ggtccggccag gctccaggga 180
aggggctgg aatggatcg aatcatggta ctccctggta cacatactac gcgaggtggg 240
cgaaaggccg attcaccatc tccaaaaccc tccggccatc gcatntgaaa atcnccagtc 300
cgacaaccga ggacacccggc acctatttct tgcggccagaga tcttcggat ggttagtagta 360
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<210> 509
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 509
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
1 5 10 15

<210> 510
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 510
Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
1 5 10 15

<210> 511
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gln Asp Gln Lys
1 5 10 15

<210> 512
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 512

Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
1 5 10 15

<210> 513
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 513

Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
1 5 10 15

<210> 514
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 514

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1 5 10 15

<210> 515
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 515
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
1 5 10 15

<210> 516
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 516
Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln
1 5 10 15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
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1 5 10 15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1 5 10 15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
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Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 520
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
1 5 10 15
Glu Ala Arg Arg His Tyr Asp Glu Gly
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<210> 521
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 521
Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1 5 10 15
Pro Pro Pro Pro Ala
20

<210> 522
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 522
Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp
1 5 10 15
Phe Thr Gln Val
20

<210> 523
<211> 254
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<220>
<221> VARIANT
<222> (1)...(254)
<223> Xaa = any amino acid

<400> 523
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Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
20 25 30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
35 40 45

Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
 50 55 60
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
 65 70 75 80
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
 85 90 95
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
 100 105 110
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
 115 120 125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
 130 135 140
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
 145 150 155 160
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
 165 170 175
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
 180 185 190
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
 195 200 205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
 210 215 220
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
 225 230 235 240
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 245 250

<210> 524

<211> 765

<212> DNA

<213> Homo sapien

<400> 524

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<210> 525

<211> 254

<212> PRT

<213> Homo sapien

<400> 525

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Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
1 5 10 15
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
20 25 30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu

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35	40	45
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50	55	60
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly		
65	70	75
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met		80
85	90	95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu		
100	105	110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu		
115	120	125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala		
130	135	140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg		
145	150	155
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu		160
165	170	175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys		
180	185	190
Ala Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly		
195	200	205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly		
210	215	220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu		
225	230	235
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser		240
245	250	

<210> 526

<211> 963

<212> DNA

<213> Homo sapiens

<400> 526

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tga
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963

<210> 527

<211> 320

<212> PRT

<213> Homo sapiens

<400> 527

Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile
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Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser
 20 25 30

Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val
 35 40 45

Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met
 50 55 60

Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile
 65 70 75 80

Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys
 85 90 95

Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr
 100 105 110

Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
 115 120 125

Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
 130 135 140

Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Pro Leu Pro Leu
 145 150 155 160

Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
 165 170 175

Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
 180 185 190

Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
 195 200 205

Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
 210 215 220

Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
 225 230 235 240

Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
 245 250 255

Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
 260 265 270

Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
 275 280 285

Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
 290 295 300

Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys

305	310	315	320
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<210> 528
<211> 20
<212> DNA
<213> Homo Sapien

<400> 528
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<210> 529
<211> 20
<212> DNA
<213> Homo Sapien

<400> 529
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<210> 530
<211> 1852
<212> DNA
<213> Homo sapiens

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<210> 531
<211> 879

<212> DNA
<213> Homo sapiens

<400> 531

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<210> 532

<211> 292

<212> PRT

<213> Homo sapiens

<400> 532

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Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
35 40 45

Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
 50 55 60

Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
65 70 75 80

Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
85 86

Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
100 105

Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
115 120

Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
130 135

Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
145 150

Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
165 170

Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
180 185 190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
195 200 205

Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
210 215 220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
225 230 235 240

Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
245 250 255

Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
260 265 270

Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
275 280 285

Val Ile Ile Met
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<210> 533
<211> 801
<212> DNA
<213> *Homo sapiens*

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ttgccaagag gcagaccata g 801

<210> 534
<211> 266
<212> PRT
<213> *Homo sapiens*

<400> 534
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130	135	140	
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln			
145	150	155	160
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg			
165	170	175	
Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly			
180	185	190	
Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val			
195	200	205	
Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala			
210	215	220	
Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly			
225	230	235	240
Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys			
245	250	255	
Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg			
260	265	270	
Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met			
275	280	285	
Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys			
290	295	300	
Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn			
305	310	315	320
Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe			
325	330	335	
Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe			
340	345	350	
Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe			
355	360	365	
Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg			
370	375	380	

Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg
 385 390 395 400
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr
 405 410 415
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser
 420 425 430
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly
 435 440 445
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro
 450 455 460
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln
 465 470 475 480
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly
 485 490 495
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala
 500 505 510
 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile
 515 520 525
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn
 530 535 540
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp
 545 550 555 560
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu
 565 570 575
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His
 580 585 590
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp
 595 600 605
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly
 610 615 620
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln
 625 630 635 640
 Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu
 645 650 655
 Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly
 660 665 670
 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu
 675 680 685

Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr
690 695 700

Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu
705 710 715 720

Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser
725 730 735

Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly
740 745 750

Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr
755 760 765

Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu
770 775 780

Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys
785 790 795 800

Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn
805 810 815

Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu
820 825 830

Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu
835 840 845

Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile
850 855 860

Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg
865 870 875 880

Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr
885 890 895

Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp
900 905 910

Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp
915 920 925

Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr
930 935 940

Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val
945 950 955 960

Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala
965 970 975

Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met
980 985 990

Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile

995	1000	1005
Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro		
1010	1015	1020
Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val		
1025	1030	1035
Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu		
1045	1050	1055
Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly		
1060	1065	1070
Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu		
1075	1080	1085
Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu		
1090	1095	1100
Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile		
1105	1110	1115
Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp		
1125	1130	1135
Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu		
1140	1145	1150
Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr		
1155	1160	1165
Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu		
1170	1175	1180
Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile		
1185	1190	1195
Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln		
1205	1210	1215
Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys		
1220	1225	
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<213> Homo sapiens		
<400> 538		
Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu		
5	10	15
Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala		
20	25	30
Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser		
35	40	45

Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val
50 55 60

Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr
65 70 75 80

Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr
85 90 95

Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr
100 105 110

Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
115 120 125

His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
130 135 140

Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn
145 150 155 160

Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro
165 170 175

Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile
180 185 190

Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln
195 200 205

Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr
210 215 220

Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile
225 230 235 240

Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile
245 250 255

Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys
260 265 270

Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile
275 280 285

Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr
290 295 300

Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu
305 310 315 320

Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala
325 330 335

Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile
340 345 350

Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His
 355 360 365
 Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr
 370 375 380
 Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val
 385 390 395 400
 Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu
 405 410 415
 Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile
 420 425 430
 Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser
 435 440 445
 Asn Ile Leu Phe Gly Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val
 450 455 460
 Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly
 465 470 475 480
 Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln
 485 490 495
 Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile
 500 505 510
 Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg
 515 520 525
 His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr
 530 535 540
 Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile
 545 550 555 560
 Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu
 565 570 575
 Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn
 580 585 590
 Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn
 595 600 605
 Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro
 610 615 620
 Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro
 625 630 635 640
 Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln
 645 650 655
 Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

660	665	670
Phe Leu Ile Leu Leu Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln		
675	680	685
Asp Trp Trp Leu Ser Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val		
690	695	700
Thr Val Asn Gly Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp		
705	710	720
Tyr Leu Gly Ile Tyr Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly		
725	730	735
Ile Ala Arg Ser Leu Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln		
740	745	750
Thr Leu His Asn Lys Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu		
755	760	765
Phe Phe Asp Arg Asn Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys		
770	775	780
Asp Ile Gly His Leu Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe		
785	790	800
Ile Gln Thr Leu Leu Gln Val Val Gly Val Val Ser Val Ala Val Ala		
805	810	815
Val Ile Pro Trp Ile Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe		
820	825	830
Ile Phe Leu Arg Arg Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg		
835	840	845
Leu Glu Ser Thr Thr Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser		
850	855	860
Leu Gln Gly Leu Trp Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys		
865	870	880
Gln Glu Leu Phe Asp Ala His Gln Asp Leu His Ser Glu Ala Trp Phe		
885	890	895
Leu Phe Leu Thr Thr Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile		
900	905	910
Cys Ala Met Phe Val Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala		
915	920	925
Lys Thr Leu Asp Ala Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu		
930	935	940
Thr Leu Met Gly Met Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val		
945	950	960
Glu Asn Met Met Ile Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu		
965	970	975

Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp
 980 985 990

Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser
 995 1000 1005

Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser
 1010 1015 1020

Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser
 1025 1030 1035 1040

Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp
 1045 1050 1055

Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys
 1060 1065 1070

Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met
 1075 1080 1085

Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp
 1090 1095 1100

Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro
 1105 1110 1115 1120

Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val
 1125 1130 1135

Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn
 1140 1145 1150

Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr
 1155 1160 1165

Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr
 1170 1175 1180

Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys
 1185 1190 1195 1200

Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr
 1205 1210 1215

Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln
 1220 1225 1230

Leu Gly Lys Ala Glu Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg
 1235 1240 1245

Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
 1250 1255 1260

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 <210> 539
 <211> 10
 <212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 539

Cys Leu Ser His Ser Val Ala Val Val Thr
1 5 10

<210> 540

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 540

Ala Val Val Thr Ala Ser Ala Ala Leu
1 5

<210> 541

<211> 14

<212> PRT

<213> Homo sapiens

<400> 541

Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
5 10

<210> 542

<211> 15

<212> PRT

<213> Homo sapiens

<400> 542

Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
5 10 15

<210> 543

<211> 12

<212> PRT

<213> Homo sapiens

<400> 543

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val
5 10

<210> 544

<211> 18

<212> PRT

<213> Homo sapiens

<400> 544

Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe

5

10

15

Met Thr

<210> 545
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Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
5 10 15

Ser Val

<210> 546
<211> 29
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<400> 546
Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly
5 10 15

Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
20 25

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<400> 547
Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu
5 10 15

Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu
20 25 30

Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
35 40 45

Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
50 55

<210> 548
<211> 18
<212> PRT
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<400> 548
Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

200

5

10

15

Glu Cys

<210> 549

<211> 18

<212> PRT

<213> Homo sapiens

<400> 549

Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg
5 10 15**Gln Ala**

<210> 550

<211> 14

<212> PRT

<213> Homo sapiens

<400> 550

Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe
5 10

<210> 551

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 551

Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
1 5 10

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